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MALIGNANT TUMORS OF THE KIDNEY IN ADULTS*

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THIS paper is based on the analysis of 50 cases of malignant tumors of the kidney in adults. Only cases that have been verified by the microscopic study of tissue removed either at operation or necropsy are included.

A great deal of controversy and confusion exists in the pathologic classification of these tumors. However, from the standpoint of clinical and roentgen diagnosis, they fall into two main groups. First, those arising from the kidney pelvis, which may be either papillary or sessile; and secondly, those arising within the kidney, the so-called "hypernephroma" or renal cell carcinoma. No attempt will be made here to classify them further.

MALIGNANT TUMORS OF THE KIDNEY PELVIS

Five of the 50 patients had tumors arising within the kidney pelvis. The involvement was on the right 3 times, and on the left twice. All these tumors were of the papillary type. Three patients were men, and 2 were women. One patient was thirty-four years of age, and 4 were over seventy.

Hematuria was the first symptom in each case. It was intermittent in character, and had been present from six months to five years before the patient was first seen. Blood clots were passed at some time by each patient. All 5 cases had a moderate secondary anemia, the average red blood cell count being 3,250,000 in the men, and 3,865,000 in the women.

One patient complained of a dull, aching pain in the flank, and 2 had colic accompanying the passage of blood clots. A palpable tumor was present in only one patient.

Kidney stones were found once, and these were in the only patient giving a history of having passed calculi. Secondary tumor implants into the bladder were found in 3 of these patients.

Roentgenograms were made on all 5 patients. While this small number is insufficient to be conclusive, it is observed that on retrograde pyelograms a small papillary tumor produces an irregular filling defect without distortion of the uninvolved portion of the pelvis, and with no distortion of the kidney outline (Fig. 1). Whether such a tumor is benign or malignant cannot be determined from the roentgenogram. While blood clots do produce defects, they tend to be smooth in outline rather than irregular as occurs with a papillary tumor.

* Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19–22, 1939.

Fig. 1. Small papillary tumor of the kidney pelvis showing an irregular filling defect, but without distortion of the uninvolved portion of the kidney pelvis or of the kidney outline.

They also can usually be ruled out by repeated washing of the kidney pelvis.

With larger papillary tumors, the pelvis may be almost completely filled with neoplastic tissue. Tumors of this size distort the kidney pelvis and may obstruct some of the calyces with resultant localized hydronephrosis. Even though the kidney pelvis is nearly filled with tumor tissue, the outline of the kidney remains intact, providing there has not been marked invasion of the parenchyma (Fig. 2).

Tumors of the kidney pelvis may, however, invade the kidney to such an extent that there is distortion of the kidney outline and a mass becomes palpable. In this event, it may be impossible to differentiate between such a tumor and a primary tumor of the kidney secondarily invading the pelvis.

In one of our cases, the ureter was found to be completely occluded by tumor tissue so that a satisfactory pyelogram could not be obtained.

Because of the high incidence of bladder implants (3 out of 5 in this series), it would seem advisable to make cystographic studies on all patients suspected of having tumors of the kidney pelvis. These secondary tumors are readily visualized on air cystograms (Fig. 3), or with opaque cystograms when the tumor is observed in profile or through a not too dense medium.

Malignant Tumors Arising Within the Kidney

Forty-five of the 50 patients had tumors arising within the kidney. Thirty-three were men, and 12 were women—a ratio of nearly three to one. The patients' ages

Fig. 2. Papillary tumor nearly filling the kidney pelvis and producing a localized hydronephrosis in the upper pole. There is no distortion of the kidney outline.

varied from thirty-three to seventy-six, the average being fifty-seven years and eight months. Two-thirds were in the fifth and sixth decades.

Hematuria was the first symptom noticed by 24 patients, although it was present at some time, but was not the first symptom, in 10 additional cases.

The hematuria was intermittent in character lasting usually from one to three days, and then disappearing for a variable period of time. Twenty-four patients gave a definite history of passing blood clots. Thirteen of these stated that they had at some time passed clots, worm-like in shape, indicating that the clots had come down the ureter.

Nearly every patient had a moderate secondary anemia. The lowest red blood cell count was 2,100,000. The average for men was 4,036,000, and for women 3,765,000.

Fig. 3. Air cystogram demonstrating a large secondary implant in the bladder wall from a primary papillary tumor of the kidney pelvis.

Fig. 4. Kidney tumor showing typical elongation and compression of upper and middle calyces.

Pain was the first symptom in 6, although it was present at some time in 24 others.

The pain complained of was of two types. First, a dull "aching", "dragging sensation", or "feeling of discomfort" in the flank noted by 17 patients. This was apparently due to streching of the kidney capsule or the weight of the tumor mass, since a palpable tumor was noted in 15 of these 17 patients. Secondly, a "sharp, colicky" pain accompanying the passage of blood clots and stressed by 13 patients. Stones were not found in any case, and only one patient gave a history of having passed calculi previously.

Tumor was the first symptom noticed by 6 of the patients. On physical examination, a tumor was palpable in 32 patients.

Loss of weight and weakness was the

Fig. 5. Large kidney tumor demonstrating elongation, narrowing, and wide separation of the major calyces.

chief complaint in 4. However, a history of loss of weight was obtained in 21 patients. In 17 of these the amount was stated and this averaged 46 pounds and took place over an average period of nine months. Twenty patients gave no history of weight loss, and in 4 no mention of weight was made in the record.

In only 2 were the first symptoms due to metastasis. One patient complained of a persistent cough and was found to have extensive lung metastasis at necropsy. The second patient developed personality changes from brain metastasis and was first committed to the psychopathic ward.

In 3 patients there were no symptoms referable to the kidney, and the tumor unsuspected during life was found at necropsy.

The duration of symptoms varied greatly. Two patients gave a history of intermittent hematuria going back over a period of fifteen years, a third for ten years, and a fourth for nine years.

Whether maligant kidney tumors can be present and produce symptoms for such a long period of time or whether the hematuria was coincidental to some unrelated cause is open to speculation. However, one patient, in whom the kidney was found to be replaced by tumor tissue at necropsy, was known to have had a palpable mass on the involved side for eleven years. A gland showing metastasis was also removed from his neck four years before death.

As previously noted, 3 patients had no symptoms referable to the kidney. Others had symptoms for only a few days or weeks before entrance. In those patients on whom

Fig. 6. Large kidney tumor showing calcium deposits. There is marked displacement of the kidney pelvis and calyces accompanied by elongation and narrowing of the calyces.

a history could be obtained, the average duration of symptoms before entrance to the hospital was twenty-five months.

The right kidney was involved 18 times, and the left 26. In one patient examined at necropsy, small, apparently primary tumors were found in the upper pole of each kidney. Of the remaining 44 patients, the upper pole was involved 15 times, the lower pole 17 and the middle or entire kidney 9 times. In 3 the location was not given in the record.

Fever has been mentioned in the past as sometimes being a remarkable concomitant symptom of renal tumors. Although specifically looked for in the records of this series, with possibly two or three exceptions, there were no patients with elevations of temperature that could not be accounted for by accompanying low-grade infection or reaction following cystoscopy. The majority of these patients, however, were under direct observation for only short periods of time.

A *B*

Fig. 7. *A*, tumor involving the central portion of the kidney. Pyelogram taken following washing out of blood clots from the pelvis. *B*, pyelogram taken before washing kidney pelvis and showing smooth filling defects due to clotted blood.

Fig. 8. Pyelogram demonstrating invasion of the kidney pelvis by tumor tissue with resulting loss of the normal outline of the pelvis and calyces.

The white blood cell counts were also for the most part within normal limits. Except for one patient with leukemia, the highest count was 23,000; only 5 were over 15,000; and the average was 9,400.

Flat films of the urinary tract and stereoscopic anteroposterior retrograde pyelograms were obtained on 34 of these patients. Additional lateral pyelograms were made in a few instances. The flat films frequently showed important positive diagnostic information such as increase in size

Fig. 9. Rarely seen deformity of kidney tumor in which there is dilatation of the kidney pelvis and calyces, but with elongation of the major calyces.

or density of the kidney, irregularity of outline, or the presence of calcium deposits.

Areas of calcification subsequently shown to be within kidney tumors were discernible on the films of 13 of the 34 patients roentgenographed. These deposits usually appeared as diffuse amorphous flecks although occasionally there were accompanying irregular plaques. Calcification was present in small tumors and appeared to bear no relationship to the size of the neoplasm.

In retrograde pyelograms, the most constant and characteristic finding was elongation and compression of one or more of the major calyces. This type of deformity was present in 23 of the 34 pyelograms. It occurs with both small and large tumors, and takes several forms. Only one or two calyces may be involved (Fig. 4), or all calyces may be elongated, compressed, and widely separated producing the so-called "spider-leg" deformity (Fig. 5). In other instances, the pelvis and calyces may be pushed to one side, but still with elongation and compression of the major calyces (Fig. 6). These changes are sometimes better demonstrated in a lateral view.

From roentgenographic observation, invasion of the kidney pelvis by tumor tissue is not a frequent occurrence. Blood clots, when present, produce filling defects which are smooth in outline and of uniform negative density (Fig. 7).

Less commonly (8 cases) there was more or less complete obliteration of the usual landmarks of the pelvis and calyces. Injected opaque material was diffused into a conglomerate mass of tumor tissue and blood clots, and produced a pyelogram characterized by the absence of any form or shape (Fig. 8).

Rarely (3 cases) the pyelogram showed marked enlargement and dilatation of the kidney pelvis and calyces, with elongation of the major calyces, but with little or no compression (Fig. 9.).

In all pyelograms, as well as on plain films, abnormalities in kidney size, contour and density should be specifically looked for.

In retrospect, in no instance was a pyelogram obtained that could be considered normal, although admittedly an elongated upper calyx from a tumor resembles a normal bifid type of kidney pelvis.

SUMMARY

Fifty cases of verified malignant tumors of the kidney in adults have been studied.

Tumors primary in the kidney pelvis were found in 10 per cent of the cases. In this group intermittent hematuria was the first symptom in each case. Accompanying stones were present only once.

There is no apparent predilection for side of involvement or sex of the patient. Secondary implants to the bladder occurred in 60 per cent of the cases.

With small and moderate sized tumors, pyelograms show irregular filling defects without distortion of the kidney outline.

Large tumors invading the kidney cannot be distinguished from primary kidney tumors invading the kidney pelvis.

Malignant tumors, primary in the kidney, were present in 90 per cent of the cases of this series. These occurred in men nearly three times as frequently as in women. The average age of these patients was fifty-seven years and eight months with two-thirds of them being in the sixth and seventh decades.

The first symptom complained of varied in different patients. Hematuria was noted by 53 per cent, pain by 13 per cent, tumor by 13 per cent, loss of weight and weakness by 9 per cent, symptoms due to metastasis by 4.5 per cent, no symptoms by 7 per cent. However, during the course of their illness most patients had more than one symptom so that hematuria was mentioned by 75 per cent, blood clots by 53 per cent, pain by 67 per cent, loss of weight by 47 per cent, and tumor was felt in 71 per cent of the patients.

The right kidney was involved in 41 per cent of the cases, and the left in 59 per cent.

In plain roentgenograms, changes in size, shape and density of the kidney, as well as calcium deposits which occurred in 38 per cent of the roentgenographed cases, should be looked for.

Retrograde pyelograms, in the presence of tumor, show most frequently elongation and compression of one or more of the major calyces. Less commonly, there may be complete loss of the normal pelvic landmarks; and rarely, dilatation of the pelvis accompanied by elongation and dilatation of the calyces without remarkable compression.*

* For discussion see page 657.

ANOMALIES OF THE URINARY TRACT*

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MUCH praise must be given to the roentgenologists for their aid to the urologists in making the diagnosis of anomalies of the urinary tract a common occurrence. It is estimated that over 40 per cent of renal and ureteral pathology, usually due to poor drainage and sepsis, occurs in the presence of anomalies of these organs. This fact makes a knowledge of the anomalous possibilities of the greatest importance.

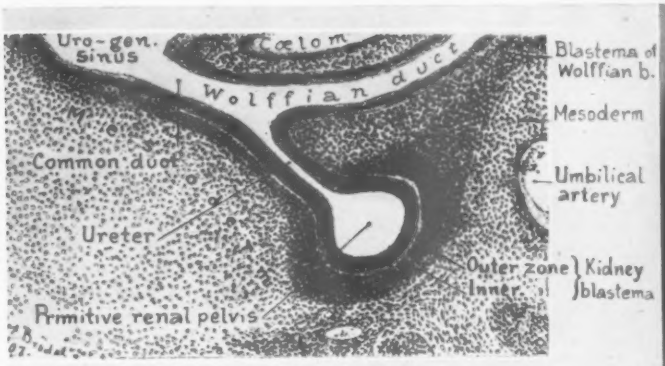
In Figure 1, it is seen that the ureterorenal bud arises on either side from the wolffian duct, near the junction of this duct with the primitive cloaca; this begins about the fourth week of embryonic life. This epithelial bud from the wolffian duct produces the ureter, renal pelvis, calyces, papillary ducts and collecting tubules; the kidney mass of cells produces the convoluted tubules, the loops of Henle, Bowman's capsules and the glomeruli. Any change in or interference with the ureteral bud or kidney blastema probably causes anomalous conditions; these changes are excessive or arrested development or are the result of fission or fusion. It is said that the tubules of the renal mass may make improper connections with the glomeruli above or the minor calyces below and remain as potential cysts through excess exudation. It is not difficult to visualize two separate ureteral buds on one or both sides to make ureteral duplication; or a fission of one ureter to make partial ureteral duplication or a double renal pelvis; or a fusion of the lower or upper poles of the kidneys to produce all kinds of fused kidneys. A great many anomalies of position undoubtedly develop when the kidney migrates from its pelvic to its permanent lumbar position; this adult kidney position is usually reached by the end of the ninth week of embryonic life. Whether dystopia is due to persistent transient blood vessels which prevent ascent of the kidneys is still debatable. Other anomalies of position are due to faulty rotation of the kidney around its longitudinal axis; the primitive pelves are originally situated ventrally and rotate to face laterally.

1. The most important anomaly of number is the absence of one kidney to produce a solitary kidney. Its importance lies in the fact that solitary kidneys have been removed due to trauma or acute pathology; uremic deaths have followed in ten to twenty-seven days. Figure 2 shows a ureteral stone which has passed down from a solitary kidney; cystoscopy revealed the absence of the right ureteral orifice and the right half of the trigone. In some of these patients there are normal ureteral orifices but one of them will end in a blind stump. Figure 3 demonstrates misinterpretation of intravenous urography in determining

* From the Urological Services of Drs. Harry Culver and William J. Baker of St. Luke's and Cook County Hospitals, Chicago, Ill. Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19–22, 1939.

Legends for Figures 1–8, next page.

Fig. 1. Embryologic derivation of ureter and kidney.
Fig. 2. Ureteral calculus from solitary kidney.
Fig. 3. Solitary kidney; low left phlebolith which was mistaken for ureteral calculus.
Fig. 4. Phlebolith.
Fig. 5. Bilateral double kidneys and ureters.
Fig. 6. Infected hydronephrosis in upper half of left double kidney.
Fig. 7. Six month postoperative pyelogram after heminephrectomy of infected hydronephrosis (Fig. 6).
Fig. 8. Extrarenal shadow and bilateral double kidneys and ureters.


Uro-gen. sinus
Cœlom
Wolffian duct
Common duct
Ureter
Primitive renal pelvis
Blastema of Wolffian b.
Mesoderm
Umbilical artery
Outer zone
Inner
Kidney blastema

LEFT
2

3

4

5

6

7

8

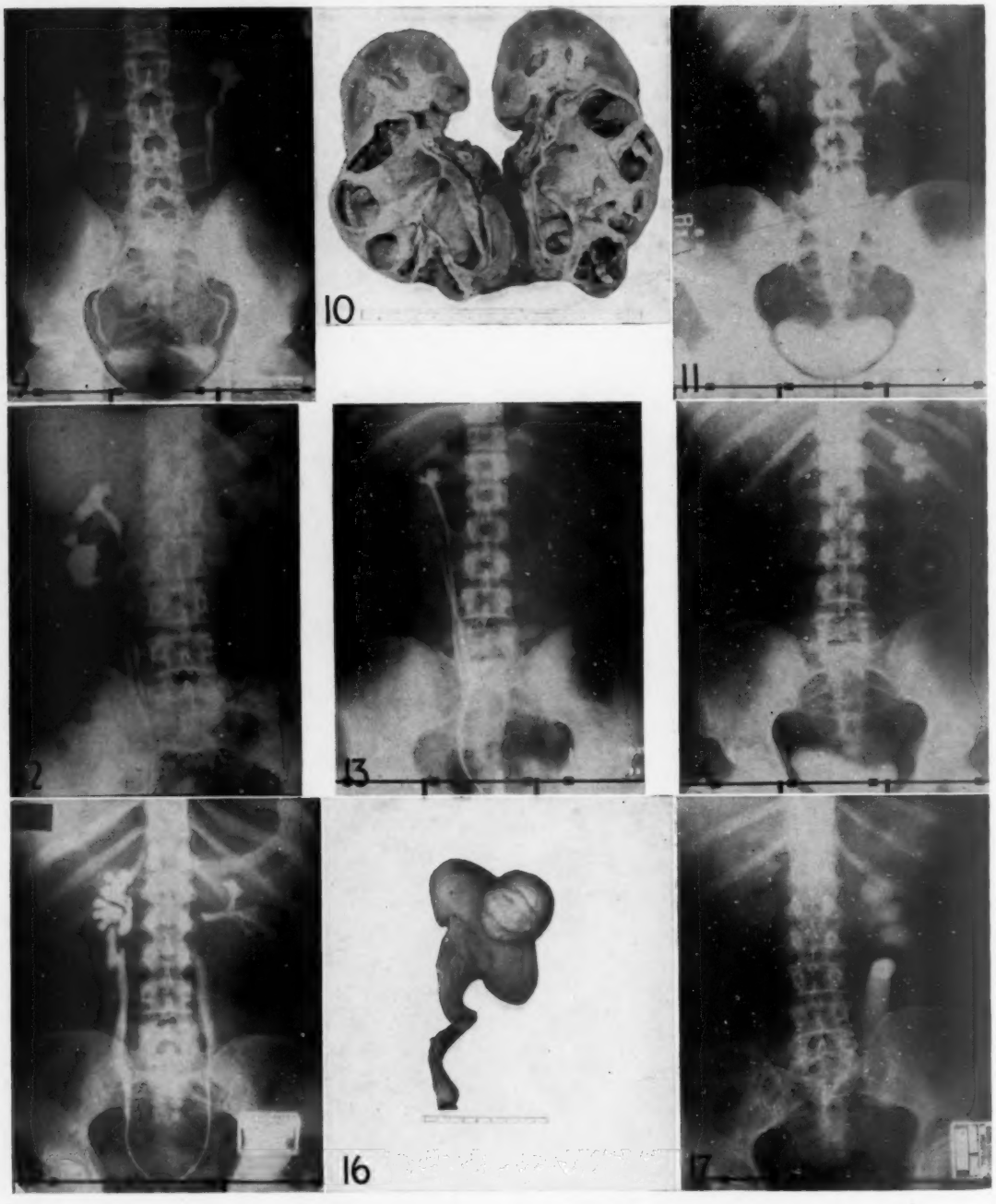


Fig. 9. Infected upper half of unilateral left double kidney.
Fig. 10. Kidney specimen of Figure 9.
Fig. 11. Unilateral right double kidney.
Fig. 12. Infected hydronephrosis of lower half of unilateral right double kidney.
Fig. 13. Calculus in lower half of right double kidney.
Fig. 14. Calculus in upper half of left double kidney.
Fig. 15. True hypoplastic infected right kidney.
Fig. 16. A renal cyst.
Fig. 17. Pyo-ureteronephrosis with no evidence of cyst in Figure 16.

the presence of both kidneys; a normal right kidney and ureter are shown; a shadow, similar to a low left ureteral stone, is seen in the region of the lower third of the left ureter; this stone was removed and proved to be a phlebolith as shown in Figure 4; later retrograde urological study proved the absence of the left kidney and ureter.

Double kidneys may occur on one or both sides. Figure 5 shows bilateral double kidneys in a female adult, who did not manifest pathology until late in life. Figure 6 shows bilateral double kidneys in an eight year old girl; the upper left kidney is an infected hydronephrosis. The upper half of double kidneys is usually the smaller of the two kidneys and the seat of more pronounced pathology. In order to be conservative, a left hemi-uretero-nephrectomy was performed and Figure 7 shows the six month postoperative pyelogram of the remaining left kidney. Figure 8 reveals bilateral double kidneys in a female adult who was subjected to urological study because of the extrarenal shadow on the right side. Figure 9 shows the upper half of a unilateral left double kidney in a boy, aged seventeen, who had had repeated left-sided colic as long as he could remember. Attention is drawn to the carnation type of pyelogram which usually indicates a double kidney. Note the constriction near the renal pelvis. This kidney was removed and the constriction was found to be caused by a moderate-sized aberrant vessel. Too many aberrant vessels prevented conservative heminephrectomy. Figure 10 is a photograph of the removed kidney. Figure 11 shows a unilateral right double kidney which was discovered when the patient was studied during a pyelitis of pregnancy. Figure 12 reveals a unilateral right double kidney in a male adult; the kidney was removed because of frequent recurrent attacks of pyelitis and an uncontrollable urinary tract infection. Figure 13 shows the right side of a bilateral double kidney of a female adult; a stone is seen in the pelvis of the lower right kidney; this kidney was removed elsewhere in 1933 because of a calcareous pyonephrosis. She consulted us in January, 1939, and a stone was found in the upper half of her double left kidney (Fig. 14). A heminephrectomy was performed.

2. A surgically important anomaly of size is the true hypoplastic kidney; its symptoms are confusing because pain and discomfort often occur in the normal but greatly hypertrophied kidney which usually accompanies a true hypoplastic kidney. Figure 15 shows a true hypoplastic infected right kidney and a large normal left kidney; the hypoplastic kidney was removed.

3. Anomalies of form of the kidney are encountered frequently. A kidney may be made wider or longer by new growths or cysts. All sizable cysts of the kidneys are probably congenital. Many of them are symptomless and are discovered with other pathological lesions. Figure 16 shows a renal cyst which accompanied a pyo-ureteronephrosis due to a low ureteral stricture which followed radium treatment of the uterine cervix. The ureteropyelogram gave no indication of the presence of this cyst (Fig. 17). Many of these renal cysts produce anomalies of position as well as of form. Figure 18 reveals a left kidney which has been pushed far toward the midline by a very large cyst; the entire kidney and cyst were removed. Cyst formation or degeneration may be entirely unilateral and produce symptoms over a long period of time. Figure 19 shows the ureteropyelogram of such a cystic kidney which was removed. The polycystic kidney which undoubtedly has a congenital impetus, produces varied and bizarre anomalies of form, in addition to nephritic findings and occasional hypertension. Figure 20 is a pyelogram of a far advanced palpable polycystic kidney; the condition was bilateral. Figure 21 is a secretory urogram of a boy, aged eleven, with bilateral polycystic kidneys; his father, who is alive and feels well, has the same condition; his deceased paternal grandfather also had the same condition. Figure 22 shows this boy's

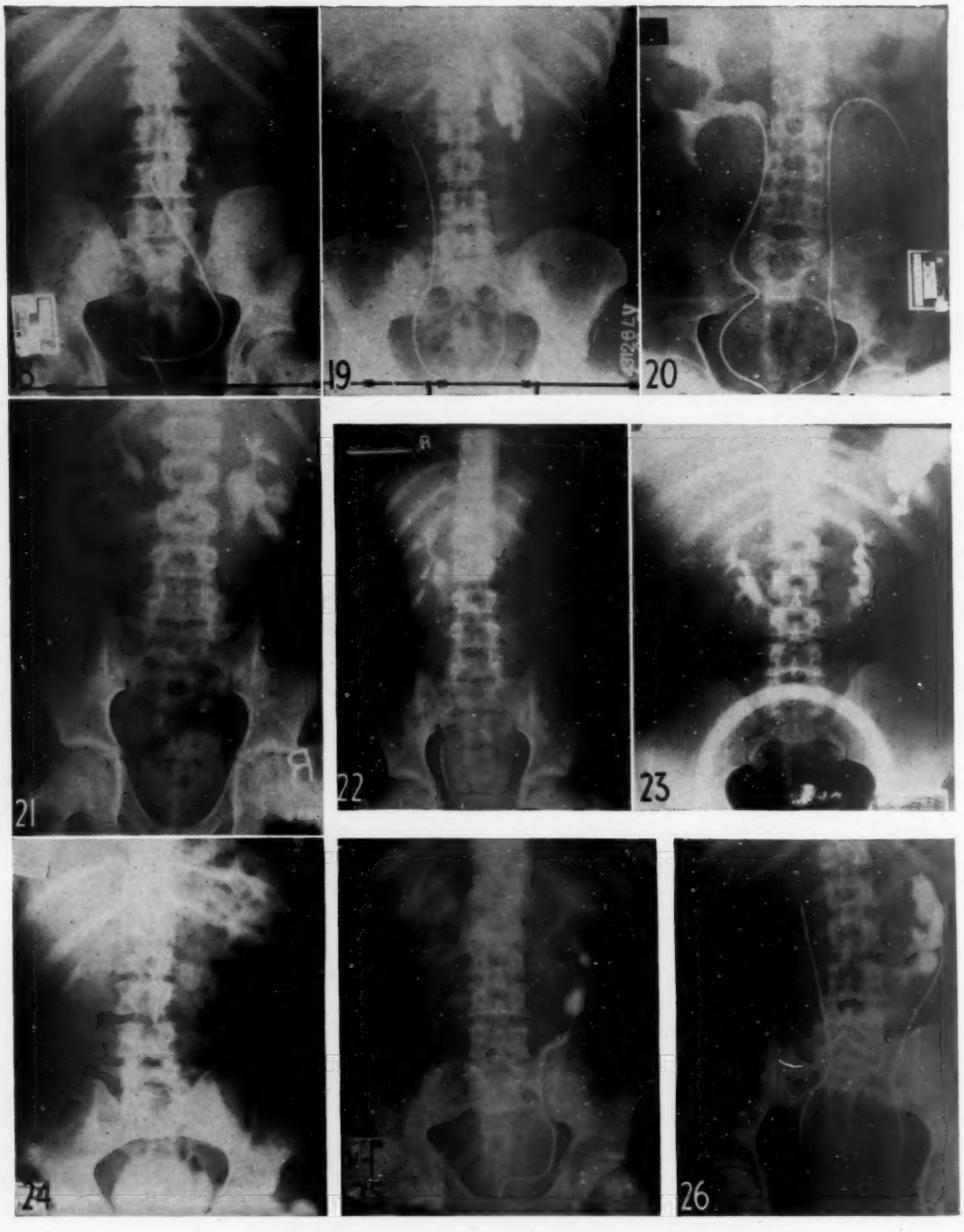


Fig. 18. Anomalous renal position due to a large renal cyst.
Fig. 19. Chronic cystic renal degeneration.
Fig. 20. Right polycystic kidney.
Fig. 21. Bilateral polycystic kidneys in a boy, aged eleven.
Fig. 22. Right pyelogram of polycystic kidney of Figure 21 two years later.
Fig. 23. Normal horseshoe kidney.
Fig. 24. Low left ureteral stone and horseshoe kidney.
Fig. 25. Calculi in left half of fused kidney.
Fig. 26. Calculus in left half of fused kidney.

right pyelogram which was taken two years later.

The symmetrically fused or horseshoe kidney produces many anomalies of form; such a kidney may manifest itself by indefinite abdominal pains, chronic constipation and urinary disturbances but its anomalous blood supply and ureteral insertions cause poor drainage so that it may become infected or harbor calculi. The hila of these kidneys usually face ventrally and medially. Figure 23 shows a normal horseshoe kidney in a male, aged twenty-six, who was operated on because of epigastric and upper right abdominal quadrant pain; it was planned to resect the isthmus of the fused kidney and suspend the right half of the kidney. Surgical inspection revealed a very large distended gallbladder and a normal horseshoe kidney. The kidney incision was closed and the gall bladder was removed later. Figure 24 shows a low left ureteral stone and the presence of a horseshoe kidney; the stone was removed and recovery was complete. Figure 25 shows two stones in the left half of a fused kidney; these were removed by anterior pyelotomy. Figure 26 shows a stone in the left half of a fused kidney; note the high insertion of the ureter and the shadow cast by the isthmus which joins the two kidneys. Figure 27 reveals a staghorn calculus in the right half of a fused kidney; a left heminephrectomy was done with complete recovery. As a general rule, removal of either half of a horseshoe kidney is difficult because of the complex and anomalous blood supply.

4. Anomalies of position should be diagnosed with reticence. If a patient knows that he has a movable or floating kidney, it will be blamed for any and all of his symptoms; many movable kidneys produce no symptoms. To diagnose ptotic kidneys, urograms must be done in flat and upright positions. Figure 28 shows third degree renal ptosis and a marked ureteral kink in a female adult; she had much pain and a persistent bacilluria. Nephro-ureterolysis and nephropexy gave complete relief. Figure 29*A* shows a movable kidney in a male adult who suffered periodic severe renal or ureteral colic; operative interference afforded him complete relief. Extrarenal encroachments produce anomalies of renal and ureteral position which are sometimes confusing. Figure 29*B* is a urogram of a female adult; a diagnosis of renal tumor was made; surgery revealed a large aneurysm of the renal artery which had displaced the kidney and ureter. Aneurysms of the renal artery are notable for a lack of audible bruit or palpable thrill.

When the normal ascent of the kidney is interfered with, an ecotopic organ results. The left kidney is usually affected. Figure 30 reveals a stone shadow which was thought to be in the urinary bladder. A cystogram proved it to be extravesical. Further study located the calculus in a left ectopic kidney; the stone was removed through a transperitoneal pyelotomy. Figure 31 shows a symptom-producing left ectopic kidney in a male adult who had undergone three laparotomies before the cause of his symptoms was discovered. Figure 32 shows a left ectopic kidney which produced pelvic pain; this pain disappeared when the infection in the ectopic kidney was cured. Figure 33 illustrates a confusing picture of a left ectopic kidney in a female adult and a round opaque partially calcified body at its superior pole; bowel study and lateral roentgenograms indicated that this mass was attached to the kidney; it proved to be a large retroperitoneal lymph gland as shown in Figure 34. Figure 35 shows a left ectopic kidney in a male adult which was so painful that a nephrectomy was done. Occasionally one sees a bilateral fused ectopia as illustrated in Figure 36. This occurred in a female adult and non-interference was advised.

5. As the kidney rises from its pelvic to its permanent lumbar position it rotates partially around its longitudinal axis so that the calyces face laterally; incomplete or exaggerated phases of this rotation produce certain anomalies of location of the calyces, pelvis, ureter and blood vessels.

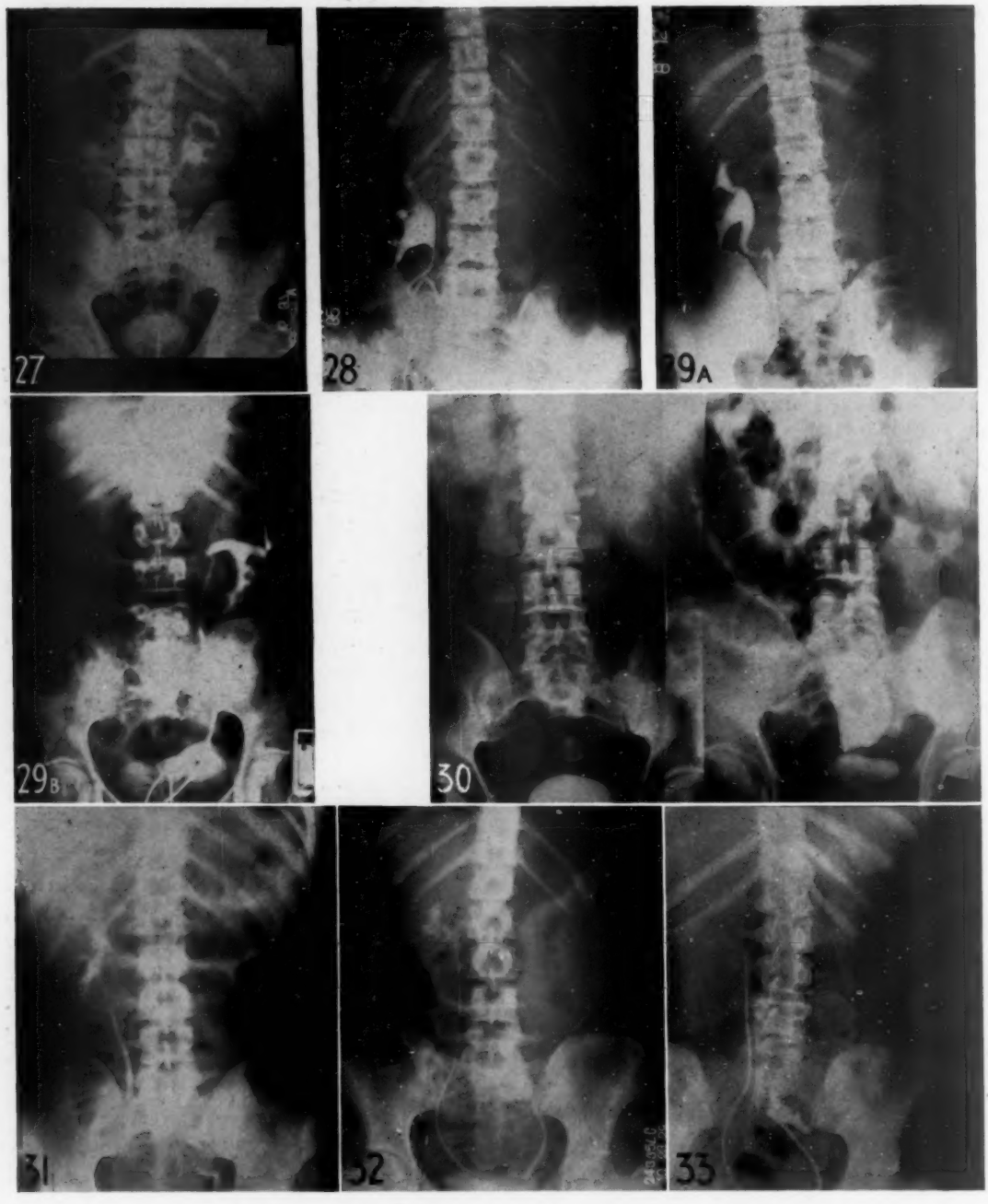


Fig. 27. Staghorn calculus in right half of fused kidney.
Fig. 28. Third degree renal ptosis in a female.
Fig. 29. *A*, third degree renal ptosis in a male; *B*, aneurysm of renal artery—diagnosed renal tumor.
Fig. 30. Calculus in left ectopic kidney.
Fig. 31. Painful left ectopic kidney.
Fig. 32. Infected left ectopic kidney.
Fig. 33. Left ectopic kidney and partially calcified retroperitoneal lymph node.

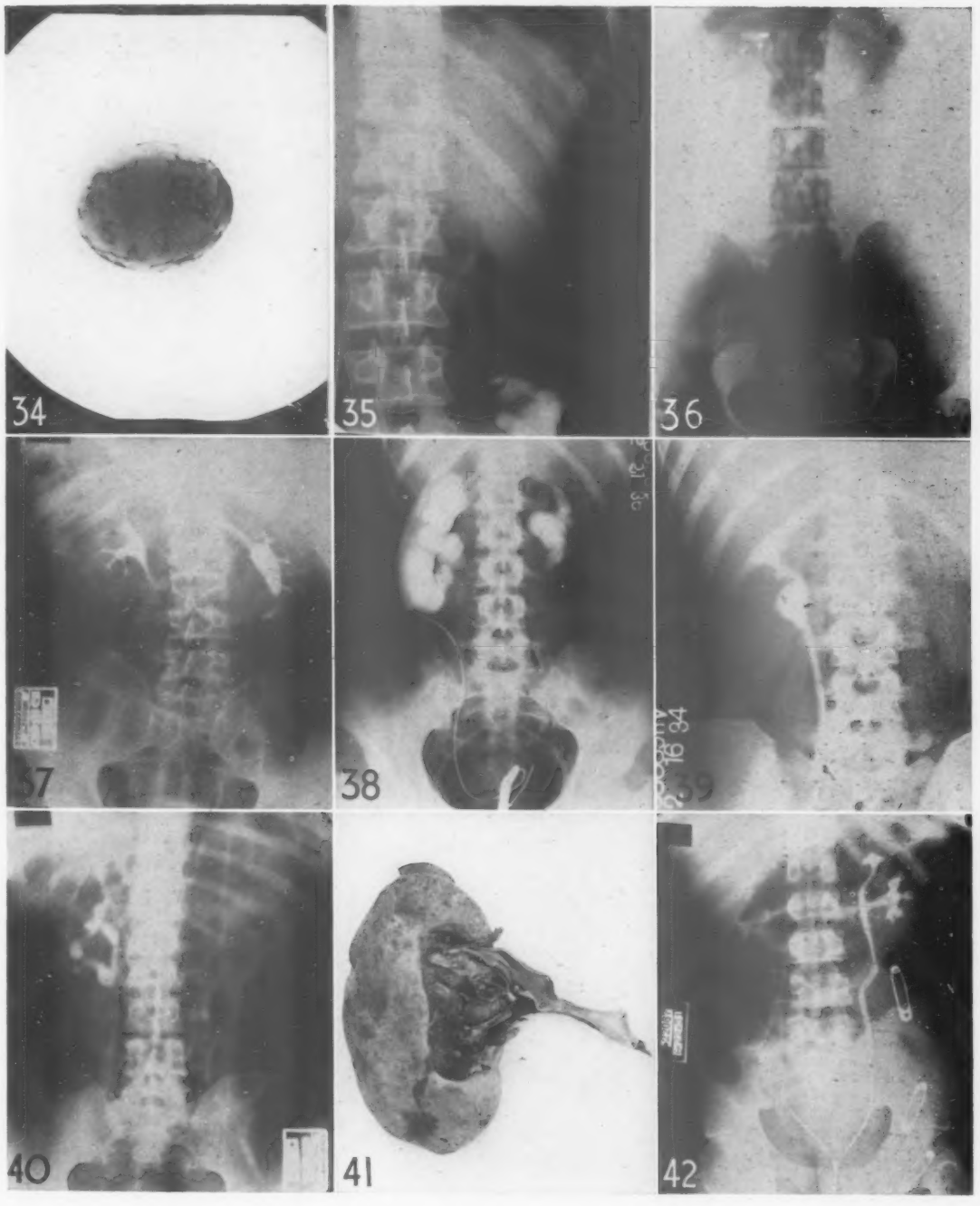


Fig. 34. Partially calcified lymph node (Fig. 33).
Fig. 35. Painful left ectopic kidney.
Fig. 36. Bilateral fused ectopia.
Fig. 37. Incompletely rotated right kidney.
Fig. 38. Incompletely rotated right kidney and abnormal insertion of ureter.
Fig. 39. Absence of some of calyces of right kidney.
Fig. 40. No true renal pelvis—extrarenal ureteral duplication.
Fig. 41. Photograph of removed kidney (Fig. 40).
Fig. 42. Bifid renal pelvis.

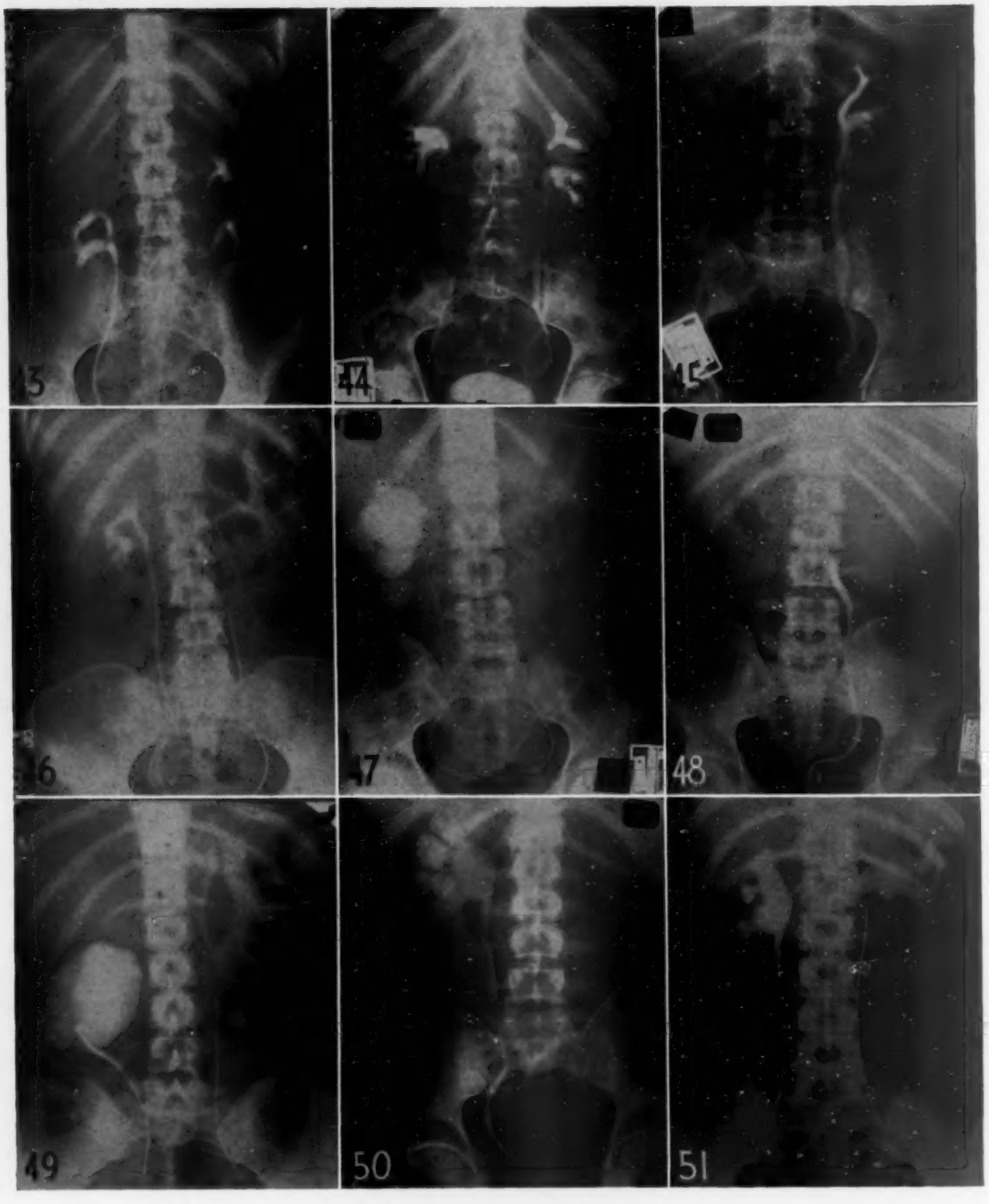


Fig. 43. Bizarre right renal pelvis.
Fig. 44. Duplication of ureter in the distal third.
Fig. 45. Stricture at site of ureteral duplication.
Fig. 46. Duplication of ureter from a juxtavesical position.
Fig. 47. High insertion of ureter to make a surgical kidney.
Fig. 48. Obstruction of ureter from intra-ureteral mucosal valves.
Fig. 49. Hydronephrosis due to congenital ureteral stricture.
Fig. 50. Hydronephrosis due to congenital ureteral stricture.
Fig. 51. Hydronephrosis due to congenital ureteral stricture.

Figure 37 shows an incompletely rotated right kidney with a stone in the renal pelvis; the stone was easily removed through a a pyelotomy. Figure 38 illustrates how incomplete rotation of a right kidney made a poor emptying angle at the ureteropelvic junction and a hydronephrosis; this kidney was removed.

6. Anomalies of the calyces, pelvis and ureter are very common.

(a) Figure 39 shows the right renal pelvis of a female adult which indicates that some of the calyces are absent. A yearly urogram for the past five years has shown the same kind of picture.

(b) Occasionally there is no true renal pelvis. Figure 40 illustrates a high duplication of the ureter, each branch ending in a major calyx, and for the most part extrarenal. The calculus was in the minor calyx. Figure 41 is a photograph of this kidney and ureter after removal. Note the definite stricture at the point of bifurcation. Figure 42 illustrates a bifid renal pelvis with partial duplication of the ureter. This was an incidental finding in a patient with a ruptured urinary bladder.

(c) Ureteral duplication is the most common anomaly of the upper urinary tract. Figure 43 reveals a bizarre right double renal pelvis and a left double kidney with duplication of the ureter. The most common site of ureteral duplication is in the upper third. Figure 44 illustrates a right infected double renal pelvis with a duplication of the ureters in the distal third. Occasionally a stricture occurs where the ureters branch; Figure 45 illustrates this point and shows a surgical kidney. Figure 46 shows a right ureteral duplication from a juxtavesical position. When ureteral duplication is complete to make two vesical ureteral orifices for one side, it is important to know that the distal orifice leads to the upper pole of the kidney and the proximal orifice leads to the lower renal pole. This occurs because the upper ureteral bud is pulled below its partner by the faster caudad movement of that portion of the wolffian duct from which it originates.

Anomalous insertion of the ureter at the renal pelvis may produce a pathological kidney. Figure 47 shows a high insertion which caused bad drainage of the renal pelvis; over a long period of time, this produced a surgical kidney in a male adult. Congenital malformations inside the ureteral lumen also cause obstructive uropathy; Figure 48 is the ureterogram of a ureter which contained a set of three mucosal valves at the point of obstruction to make a large, painless but infected surgical hydronephrotic kidney. Figures 49, 50 and 51 illustrate surgical hydronephroses due to congenital ureteral strictures, so termed by the pathologists who examined the removed specimens; all occurred in adults.

(d) Anomalies of size of the ureter are usually associated with infection and the ureterectasis has a definite relation to the infection. Figure 52 shows bilateral dilatation of the lower third of the ureter in a female adult with no apparent obstruction but much infection; the kidneys show moderate pyelectasis. The so-called idiopathic large ureter probably has a defective anatomical and neurological basis. Figure 53 illustrates a huge idiopathic hydro-uretero-nephrosis with some dilatation of the opposite ureter in a female adult. Since these dilatations tend to be bilateral, both sides must be studied if surgery is contemplated.

Another anomaly of size of the ureter is illustrated in those patients with ureterocele, which is a cystic dilatation of the lower end of the ureter, with varying amounts of bulbous dilatation of the lower ureter and little or no dilatation of the renal pelvis. Most of these swellings have a very small ureteral orifice. Figure 54 shows the ureterogram of a female adult with a ureterocele, which was discovered when she was examined for a recurrent pyelitis; Figure 55 shows the same finding in a male adult. Ureteroceles may be bilateral and persist over such a long period of time that stasis and infection invite the formation of calculi. Figure 56 illustrates

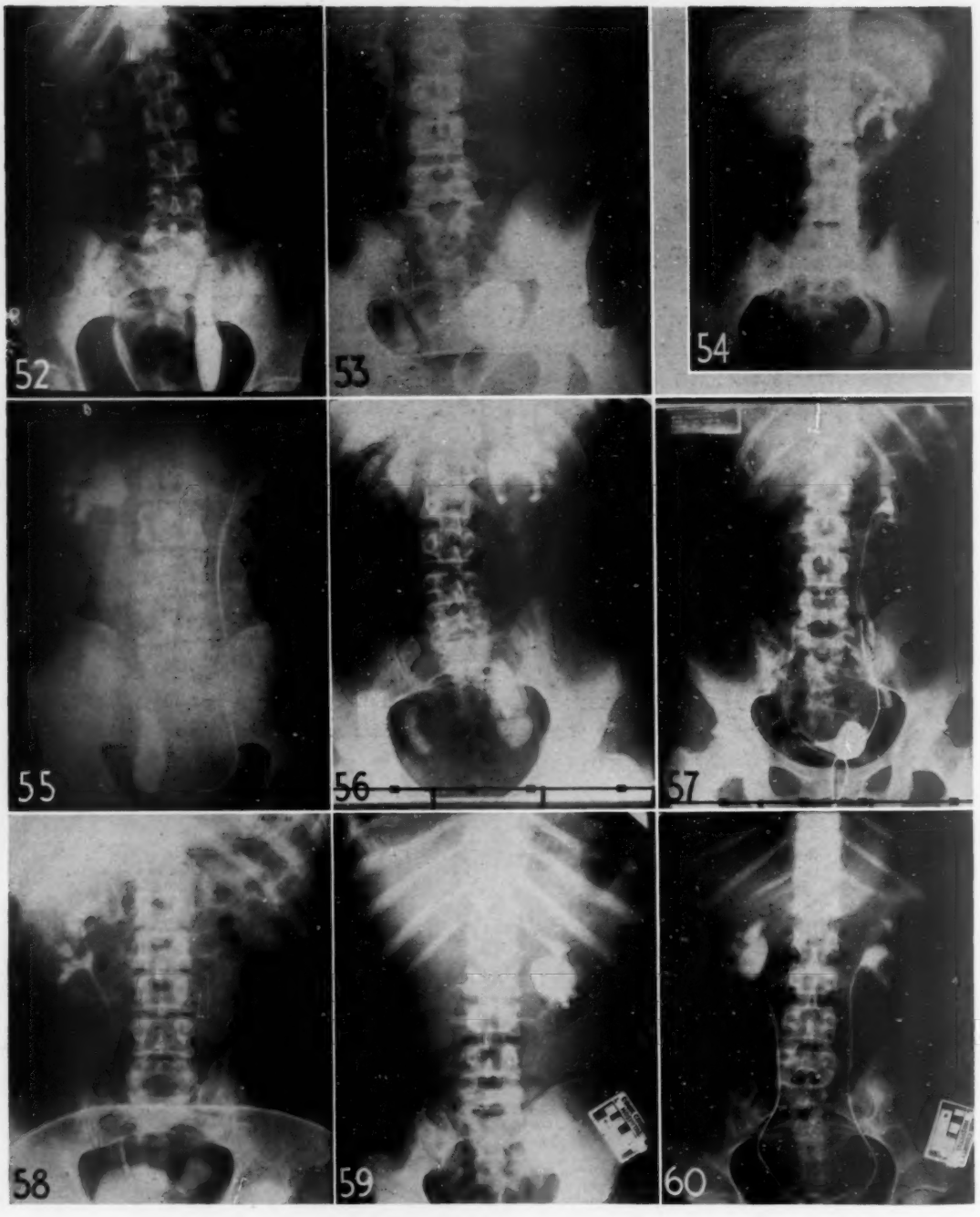


Fig. 52. Idiopathic dilatation of lower ureters.
Fig. 53. Huge idiopathic hydro-ureteronephrosis.
Fig. 54. Left ureterocele in a female.
Fig. 55. Right ureterocele in a male.
Fig. 56. Bilateral ureterocele and multiple urinary calculi.
Fig. 57. Left ectopic ureteral opening into vagina.
Fig. 58. Left ectopic ureteral opening into a seminal vesicle.
Fig. 59. Hydronephrosis and aberrant renal artery.
Fig. 60. Hydronephrosis and aberrant renal artery.

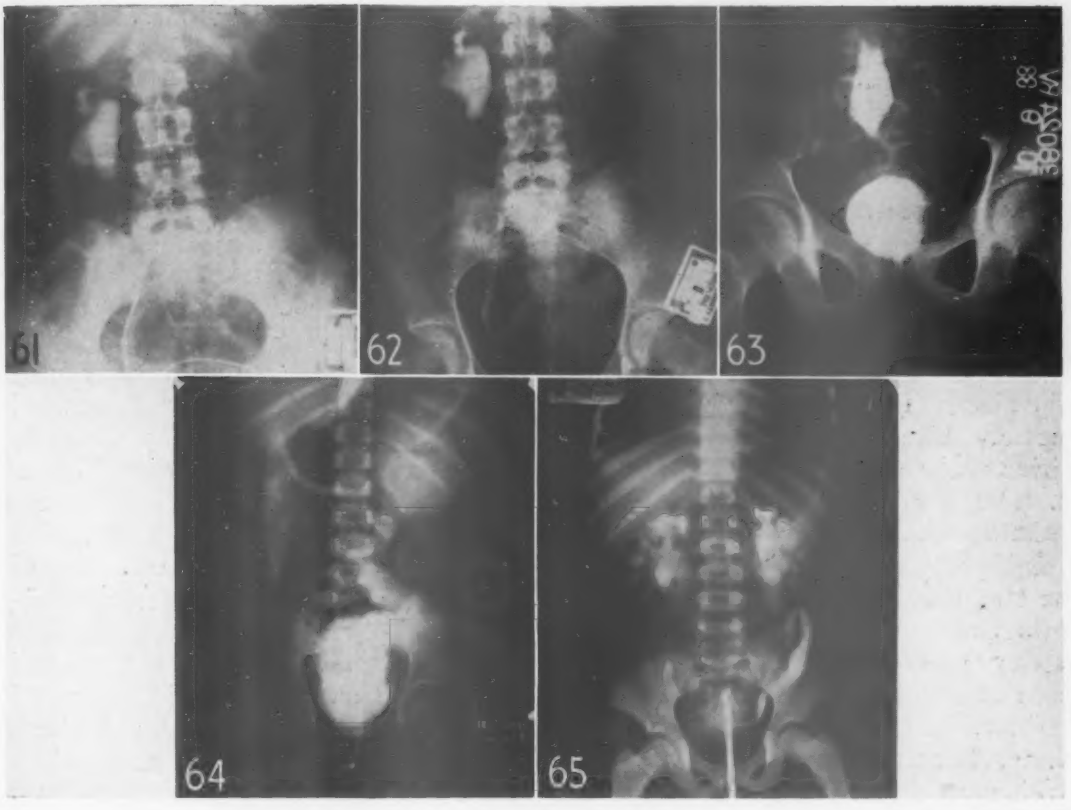


Fig. 61. Hydronephrosis and aberrant renal artery before section of vessel.
Fig. 62. Hydronephrosis and aberrant renal artery after section of vessel.
Fig. 63. Urachal cyst.
Fig. 64. Hydro-ureteronephrosis and congenital urethral valves in a boy.
Fig. 65. Hydro-ureteronephrosis and contracture of the vesical neck in a boy.

bilateral ureterocele formation and calculi in both kidneys and one ureter.

(e) Anomalies of position of the lower end of the ureters may not be discovered until adult life is reached, in spite of the incontinence of urine and much inconvenience. Figure 57 is the urogram of a female adult with a completely duplicated left kidney and ureter, with the lower left ureteral orifice ectopic in the vaginal introitus; the lower end of the ectopic ureter was dilated but the kidney was not infected. The kidney did not lend itself well to a heminephrectomy, so a complete ureterectomy of the ectopic ureter was done with an uneventful recovery. Figure 58 is the urogram of a male adult with complete duplication of the left ureter and kidney but one of the left ureters opens extravesically into the left seminal vesicle; when indigo carmine is injected intravenously, it appears in spurts from the verumontanum. This patient suffers from a chronic urinary tract infection.

7. One cannot leave the subject of the anomalous kidney and ureter without directing attention to the anomalous blood vessels which supply many kidneys. Whether the aberrant vessels cause pathology is still debatable; however, renal and ureteral symptoms and pathology are found in the presence of aberrant vessels and must, in most instances, be considered related. Figure 59 shows a left hydronephrosis in a male adult which was apparently caused by an aberrant artery; section of vessel gave complete relief from previous symptoms and pyelectasis. Figure

60 illustrates the same finding in a young female adult with periodic acute symptoms; this kidney was removed. Section of an aberrant renal vessel may relieve the symptoms of obstruction without changing the hydronephrotic picture. For example, Figure 61 shows a hydronephrosis and aberrant vessel preoperatively and Figure 62 is the postoperative urogram of the same patient. Care must be used in the section of these vessels; to cut one which supplies too much renal substance invites necrosis of the kidney. It is wiser in some instances to cut and transplant the ureter to a new position of the renal pelvis.

8. (a) Regardless of the controversy as to whether the urachus is the remains of the embryological allantois or is sometimes a part of the formed bladder which has been pulled up to the umbilical region, interesting anomalies occur in this region. Figure 63 shows a cyst of the urachal region; there was a constant discharge from the navel but there was no connection with the urinary bladder. The cyst was removed.

(b) There is some doubt as to whether vesical diverticula are congenital outpouchings which are aggravated by vesical neck obstruction or whether they are blown out portions of a worn out bladder wall back of a long standing obstruction. The fact that vesical diverticula are found in the newborn has led to the supposition that they could originally be a budding from the wolffian duct, similar to the formation of the ureteral bud. This theory is attractive because almost all diverticula occur in the region of the ureteral orifices.

(c) Anomalies of the vesical outlet are important because of their obstructive character and resulting uropathy. Figure 64 is the urogram of a boy with congenital urethral valves. Note the pyelo-ureteroectasis of a marked character. Figure 65 illustrates bilateral infected hydro-ureteronephrosis in a boy, aged eight, with a congenital bar or contracture of the vesical neck; this obstruction was resected with a good clinical recovery.

Time does not permit a complete review of the anomalies of the urinary tract but the above discussion will emphasize the fact that much uropathy occurs in the presence of these anomalies and that urography is indispensable in the diagnosis and treatment of these conditions.*

* For discussion see page 657.

Vol. 43, No. 5

URETERAL OBSTRUCTION*

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URETERAL obstruction with resultant hydronephrosis should be a subject of the utmost importance to the roentgenologist as such a lesion may produce symptoms easily ascribed to other abdominal complaints or to pathologic change in the spine. Every roentgenologist should think of this possibility in suspected gastroenterological problems, particularly if examination of the spine and gastrointestinal tract is negative. This type of examination is as easily accomplished as an intravenous examination of the gallbladder. By such investigations, many otherwise undiagnosed kidney lesions may be definitely exposed.

Intravenous urography should constitute one of our major methods of examination and should be used as frequently as most other examinations. In a recent review of a great number of cases of ureteral obstruction, we were amazed to find that a high percentage of cases had markedly advanced lesions and that a vast number had been submitted to operations directed to other organs without relief of the symptoms. This applies particularly to patients without abnormal change in the urine or without bladder symptoms.

We hope by this discussion to make more men "kidney conscious," with the result that a correct diagnosis may be made earlier and more often. This is of particular importance when ureteral obstruction is present, either partial, or complete and continuous, or intermittent. Damage to the kidney will result on the affected side, and often infection from retention or the formation of kidney stones, and eventually destruction of a kidney.

In order to appreciate more fully the cause of these changes, it is pertinent to review briefly the anatomy, physiology, and innervation of the ureter. I would like to impress on the roentgenologist the ever-increasing necessity of a better understanding of neurological symptoms which play so great a part in the diagnosis of almost all diseases. This applies particularly to pain and its distribution. The ureter is a flattened tube which extends from the outlet of the kidney pelvis to the angle of the vesical trigone where it empties into the bladder. It may enter the bladder at almost a right angle to the wall or it may enter in a rather marked oblique course. The ureter is composed of three coats—a fibrous outer coat, a muscular middle coat, and an inner epithelial coat or mucosal lining—underneath which lies a layer of submucosal tissue composed of elastic fibers and connective tissue. The middle or muscular coat is composed of unstriped fibers.

The vascular supply of the ureter is abundant, being derived from several sources, and it is freely anastomosing. The renal artery supplies the upper third of the ureter; branches from the aorta and common iliac, the inferior mesenteric or spermatic supply the middle third, while the lower third is supplied from the vesical arteries and the vas.

The nerve supply of the ureter is also very important in ureteral obstruction and particularly in the study of referred pain. The nerve supply is an intricate meshwork of small fibers. The outer fibrous sheath of the ureter carries the nerve supply, the innervation coming mainly from the renal, spermatic, ovarian, and hypogastric plexuses. The vesical plexus also supplies a portion of the lower end of the ureter. The afferent fibers come from the tenth and eleventh thoracic vertebrae, and the first lumbar vertebra. The efferent fibers are also in the vagus supply to the ureter. A few ganglia are found in the lower third of

* Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19–22, 1939.

the ureteral segment. The definite anatomical structure of the innervation of the ureter, however, has not been accurately demonstrated. It is interesting experimentally, however, that all the nerves supplying the ureter may be cut and yet its contractions appear to continue normally. Even a cut section, completely taken from the ureter, is seen to contract rhythmically after removal, and little influence can be induced in the ureter by stimulation from the hypogastric nerves or by the administration of adrenalin. There is no sphincter at the lower end of the ureter; apparently it is closed by the contraction of the bladder wall and, it is believed, by a reflex contraction of the lower portion of the ureter.

The results of partial or complete obstruction to the ureter must be understood if correct diagnoses and treatment are to be instituted. It has been shown that, if the ureter is completely obstructed permanently, atrophy and nonfunction of the kidney take place. Intermittent or partial obstruction results in a marked dilatation of the kidney, causing hydronephrosis and accompanying pain and urinary stasis which results in infections and often in the formation of renal calculi.

From a clinical standpoint, pain is usually the first symptom of any degree of obstruction that overdistends the pelvis of the kidney. Because such pain may be referred to the gastrointestinal tract and simulate spastic colon, or to the region of the gallbladder simulating gallbladder colic, and because it may simulate lesions of the spine, angina pectoris, and many other symptoms, the pain of hydronephrosis may continue for a long time before its true etiology is determined. It may be stated quite truthfully that hydronephrosis may present no characteristic symptoms and may be recognized only by inference. Therefore, one should always bear in mind the possibility that such a condition may be present. Since early hydronephrosis may cause no abnormal change in the urine, attention is often not directed to the possibility of ureteral obstruction.

For a number of years it has been our policy to make a careful examination of the abdomen in order to determine the size and shape of both kidneys, as well as the presence or absence of visible calculi before any examination is made with opaque media for a study of the gallbladder or gastrointestinal tract. It has been possible by this procedure to determine in a large number of cases the presence of a stone, either in the kidneys or ureter, which had heretofore been unrecognized, to discover the presence of a tumor of the kidney as shown by the abnormal change in the contour of this organ, and also to determine the presence of a large kidney on one side suggesting the presence of hydronephrosis. We consider this procedure to be very important and we advise that all patients who are suffering from abdominal pain have such an examination made as the first roentgenological diagnostic procedure.

The causes of ureteral obstruction are many. Among the more frequent causes may be considered:

A. *Lesions of the kidney*
   1. Renal calculi
   2. Tumor
   3. Infections
   4. Blood clots
   5. Anomalous renal vessels
   6. Anomaly of position
   7. Duplex kidney
   8. Fused kidney

B. *Lesions of the ureter*
   1. Ureteral calculi
      Opaque
      Nonopaque
   2. Stricture
   3. Tumors
      Primary
      Secondary
   4. Trauma
      Ligation
      Cutting
   5. Infection
   6. Adhesion
      Congenital
      Acquired

7. Kinks
8. Congenital valves
9. Diverticulum
10. Duplication
11. Transplanted ureters
12. Ureterocele
13. Atrophic ureter
14. Megalo-ureter
15. Ectopic ureter
16. Extrinsic pressure
17. Pregnancy

C. *Lesions of the bladder*

1. Tumors
2. Diverticulum
3. Infarction
4. Trauma

The lesions of the kidney offer a special group for diagnosis as many of these ureteral obstructions are secondary to a primary lesion in the kidney. These examinations will be better made by a pyelogram of the kidney by the retrograde method. Some tumors (Fig. 1) and anomalies such as aberrant vessels (Fig. 2), fused kidneys and malposition will usually be readily diagnosed from a urogram made by the excretory method providing there is a reasonable function in the kidney on the affected side. Hematuria may offer a difficult problem. Repeated examinations or examination during intervals of nonbleeding will often be necessary.

Fig. 1. Female, aged fifty-two. Bilateral pyelogram shows a normal right kidney with a large tumor mass in the lower pole of the left kidney producing some intermittent obstruction and a moderate hydronephrosis. Postoperative diagnosis was solitary cyst of the kidney.

Fig. 2. Male, aged thirty-one. Retrograde pyelogram shows a large hydronephrosis of the left kidney due to an aberrant vessel obstructing the upper end of the ureter. Operation: nephrectomy. The kidney was almost totally destroyed.

It is a foregone conclusion that most ureteral obstructions must be accompanied by pain during the attacks of distention of the kidney pelvis. If there is complete continuous obstruction, the kidney will cease to function and there may be no pain present due directly to the ureteral obstruction. If, however, there is an accompanying

FIG. 3. Female, aged thirty-nine. Retrograde pyelogram shows a fused ectopic kidney with bilateral ureteral obstruction.

kidney lesion, pain may be present from this source. It is also possible for a tumor of the kidney to be present without pain or hematuria, the latter being absent in about 53 per cent of kidney tumors in our series.

The poor function of polycystic kidneys will often make it impossible to determine the presence or absence of this disease, and retrograde pyelography will be necessary. A fair estimate of function will be determined, however, by the excretory urogram. The fused kidney (Fig. 3) offers obstruction to the ureters by pressure on the upper third and may be accompanied by a chain of symptoms, the so-called horseshoe kidney syndrome described by Gutierrez.[1]

Horseshoe syndrome

a. Abdominal pain in the epigastrium or the region of the umbilicus
b. Chronic constipation with or without gastrointestinal disorder
c. Urinary disturbance

Renal calculi (Fig. 4) will often be best apprehended by excretory urograms and the degree of ureteral obstruction determined from the presence of distention or retention at the one hour period. At the same time, the position of the stone will be seen and its location established, while often the retrograde pyelogram will entirely obscure the stone shadow.

This briefly surveys the best plan of examination in the presence of the lesions confined to the kidney. In the majority of all these lesions other methods of examination are helpful and should be done. Certainly, in any questionable case, excretory urography should be followed by a

FIG. 4. Male, aged forty-six. Low back pain for six months. Excretory urogram at thirty minute period shows exact location of a stone in the right kidney pelvis with a little hydronephrosis in the kidney.

retrograde pyelogram. For examination of lesions in the ureter, both catheterization of the ureter and pyelo-ureterograms may be necessary as excretory urography will not often visualize the ureter well. The presence of retention and obstruction and interference of the dynamics of the ureter will be clearly determined, however, and further study of the ureter can be made.

In the examination of a patient with ureteral calculi (Fig. 5), if there is not a complete obstruction by the stone and a functioning kidney is present, excretory urography often offers all the diagnostic information necessary before manipulation or operation is undertaken. The neurological findings of pain and distribution are of aid in locating a nonopaque stone which may also be determined by a nonopaque shadow either in the kidney pelvis or in the ureter, care being taken to exclude an air bubble which may be introduced with the pyelographic medium.

Fig. 5. Male, aged thirty-seven. Right ureteral stone. Urogram shows hydronephrosis, intermittent ureteral obstruction. The urogram, one hour period.

Fig. 6. Male, aged thirty-four. Stricture of left ureter at ureteropelvic junction. Ureterogram shows partial obstruction with a large hydronephrosis. Plastic operation done. Excretory urogram at thirty minute period.

Ureteral stricture (Fig. 6). This lesion probably occurs more often in the middle or lower portion of the ureter and may produce partial or complete obstruction. Urologists disagree somewhat on the frequency of occurrence of this lesion. We believe, however, that the presence of spasm of the ureter or spastic contraction may often be mistaken for an organic stricture. We have proved that such was the case where catheter obstruction, suggesting a stricture, was ruled out by a later urogram with four films, showing the suspected area in the ureter to be normal and with no evidence of dilatation of the kidney pelvis, ruling out any apparent ureteral obstruction.

Ureteral tumors, primary or transplant

FIG. 7. Male, aged sixty-three. Hematuria one year's duration. No other urinary symptoms. A ureterogram of the right side shows an obstructive lesion about the mid-ureter. This was a primary papillary carcinoma of the ureter.

lesions (Fig. 7) produce obstruction of the ureter with an accompanying hydronephrosis and hematuria and in the transplant lesion a primary tumor will be found in the accompanying kidney.

FIG. 9. Male, aged fifteen. Retrograde pyelogram showing bilateral hydronephrosis, bilateral ureterectasis, with bilateral congenital valve at the lower end of the ureters. Patient has renal rickets.

Trauma, either injury or surgical accident or radiation stenosis, may safely be studied by excretory urography if extravasation is present; although the kidney may rupture, no harm can be done.

FIG. 8. Female, aged thirty-four. Diagnosis, ureteral obstruction at ureteropelvic junction. Pyelonephrosis right kidney. Urinary symptoms one year. Operation: nephrectomy.

Fig. 11. Male, aged fifty-four. Cystogram shows diverticula of bladder with one diverticulum near the lower ureteral orifice on the left, producing partial obstruction to the ureters.

Ligated or crushed ureters show no function.

Infections (Fig. 8). Most infections will be accompanied by pus in the urine and frequently by blood. Such cases are best

Fig. 10. Male, aged seventy-six. Excretory urogram at thirty minute period shows the right kidney with a double ureter and kidney pelvis and hydronephrosis.

examined by a catheterization of ureters and retrograde pyelogram.

Adhesions to the upper ureter may simulate very closely an aberrant vessel obstruction at the ureteropelvic junction and it will be found impossible in many cases to

Fig. 12. Male, aged fifty-nine. Catheterization of right ureter with a ureteropyelogram, showing a large ureterocele at the lower end of the right ureter, producing partial obstruction of the ureter.

FIG. 13. Transplanted ureters (transplanted at nine years of age). Female, aged twenty-nine. Both kidneys apparently normal size with good function. Large quantity of urine and dye in colon showing good retention.

differentiate between these lesions by roentgen examination. Kinks and congenital valves will be well visualized by the excretory urogram; ureteral valves (Fig. 9) are usually bilateral and if catheterization of the ureter is done the catheter will be introduced into the ureter from below unobstructed.

Duplication of the ureter (Fig. 10), if not completely to the bladder, will often produce a partial obstruction at the joint of bifurcation confined usually to one leg of the bifurcation. It will usually be necessary to do a ureteropyelogram to visualize well such a lesion.

The excretory urogram is often the procedure that shows a double kidney pelvis and will be the first suspicious finding.

Diverticulum (Fig. 11) and ureterocele (Fig. 12) are both rare lesions and can usually only be found by a retrograde pyelo-ureterogram. However, they should be kept in mind and if any unusual finding arises on an excretory urogram, instrumental urography should immediately be recommended.

Transplanted ureter with obstruction can only be studied by excretory urograms (Fig. 13); also this is the best method for the examination of the dilatation of the ureter in pregnancy, The atrophic obstruction of the ureter in polycystic kidneys is difficult to detect at all by excretory urograms as usually these kidneys have a poor function. The ectopic ureter will require a retrograde pyelogram or ureterogram.

Megalo-ureter will usually be visualized well by the excretory urogram. Extrinsic pressure on the ureter will also usually be determined well by the excretory urogram. Many lesions of the bladder are best in-

FIG. 14. Male, aged thirty-four. Urinary symptoms for three years. Miliary tuberculosis of the lungs. Tuberculosis of the bladder with urinary obstruction. Excretory urogram at thirty minute period.

vestigated by cystoscopic examination, except for possible diverticula. In the presence of a diverticulum with the ureter entering such a lesion, a cystogram will often be of greatest aid. Tuberculosis of the bladder may be studied by a urogram (Fig. 14).

This brief consideration of ureteral obstruction will call attention to the great variety of possibilities and call our attention to the necessity of thorough examination, if the roentgenologist is to become a proficient diagnostician.

The urologist will be the judge as to diagnosis and management. The clinical history and the urological findings combined with roentgenological findings are all necessary in the final diagnosis.

DISCUSSION OF PAPERS BY DRS. GILLIES, BAKER, AND NICHOLS

Dr. Herman L. Kretschmer, Chicago. The essayists have covered the various assignments in a very thorough and comprehensive manner. I should like to discuss these papers from the point of view of some of the diagnostic problems that I have met in this particular field. I will illustrate my remarks with lantern slides.

(Slide) We are generally accustomed to believe that when a patient has a tumor of the kidney, certain more or less characteristic changes are found in the pyelogram and this impression as a broad, general proposition is true. On the other hand, one may occasionally see a patient who has a tumor of the kidney and the pyelogram is normal. In this case an infant had a tumor of the kidney that in its growth did not invade nor compress the renal pelvis and the pyelogram as you see was normal. I think one must bear this possibility in mind so as not to come to wrong conclusions. This was a Wilms' tumor, and, as I said before, it had not compressed nor invaded the kidney pelvis; hence the pyelogram was normal, so unless we think of this remote possibility, we are likely to be led astray.

(Slide) This slide shows a double kidney pelvis and a double ureter, of which you have seen many examples this morning. The reason I show this slide is to call your attention not to this anomaly *per se*, but to the frequency with which it is incorrectly diagnosed. Patients who have this anomaly are told that they have an extra kidney and cases of this type have been diagnosed as supernumerary kidneys. Supernumerary kidneys mean the presence of three separate and distinct kidneys. These patients do not have three kidneys. They have two kidneys. They have a double kidney on one side and a normal kidney on the other and at other times the lesion is bilateral, several examples of which we have just seen. It is interesting to note how frequently cases are reported as supernumerary kidneys when the author's illustrations clearly show that he is reporting cases of double kidney.

(Slide) This is a case of true supernumerary kidney. On this side the pyelogram is normal. On the opposite side you will note that there are two separate and distinct pelves widely separated. This patient actually had three separate and distinct kidneys with a free interval between them. The kidneys were not connected as is the case in double kidney. This diagnosis was verified by operation. As you all know, these cases are very rare; nevertheless we should be accurate in the use of descriptive terms, when reporting cases of this kind.

(Slide) There seems to be a little difficulty at times in the diagnosis of polycystic kidney. Polycystic kidney has frequently been confused with malignant tumor. Occasionally it is quite difficult especially in the early cases to make the differential diagnosis. One must also bear in mind the fact that the patient with a polycystic kidney may occasionally have a malignant tumor in that polycystic kidney. There should be no difficulty in recognizing this as the pyelogram of polycystic kidney.

(Slide) Most urologists believe that they are always bilateral. Here is a pyelogram from which a diagnosis of polycystic kidney was made elsewhere and the patient treated for several years as a case of bilateral polycystic disease of the kidney. This patient has a peculiar pyelogram but careful study of this pyelogram shows that there is a trickling of the medium toward the upper pole and one should have no difficulty in diagnosing this a malignant tumor. A diagnosis of hypernephroma was made and verified by operation. The patient subsequently died of brain metastasis. The point is, this was a pyelogram of a tumor incorrectly diagnosed as a polycystic kidney, and the patient was treated medically for three or

four years before the final and correct diagnosis was made.

(Slide) This shows an intravenous urogram and it is an exceedingly interesting one. One is at once impressed by the great length of the pyelograms as well as by the somewhat bizarre appearance. A large easily palpable mass was present in both right and left upper quadrants. The patient, a child, had a splenomedullary leukemia with leukemia infiltration of both kidneys, which accounted for these peculiar pyelograms. I show them because of their close resemblance to the pyelograms of a polycystic kidney with which condition they might be confused.

(Slide) Occasionally the problem of differential diagnosis may arise between tumors of the kidney and retroperitoneal tumors. In this group of cases one must resort to the use of the cystoscope, ureteral catheters and pyelograms. In this instance the patient had a peculiar shadow, as you can see it was irregularly dense. There was displacement of the ureter. At operation a retroperitoneal lipo-fibrosarcoma was found.

(Slide) This is the pyelogram of another patient with a retroperitoneal tumor and it shows in a very clearcut manner the displacement of the ureter as a result of the growth of the tumor. Displacement of the ureter is relatively frequent in cases of retroperitoneal tumor.

(Slide) Attention was called this morning to the fact that the presence of blood clot in the renal pelvis may be confused with tumor of the pelvis or tumor of the kidney proper. In this patient the filling defect was due to the presence of a very large blood clot in the kidney pelvis.

(Slide) Sometimes a differential diagnosis between a solitary cyst and malignant tumor of the kidney may be exceedingly difficult. In some of the cases of solitary cyst the intravenous urologrames show progressive increase in the density of the shadow produced by the cyst after the cyst becomes filled with the contracting fluid. Unfortunately, this is not always present. A filling defect produced by a solitary cyst many times closely resembles the filling defect produced by a tumor.

Dr. T. P. Grauer, Chicago. In regard to malignant tumors, the films that were shown and demonstrated were very beautiful and, in most instances, very obvious. The thing that seems important to me is that in many instances urological pictures do not clearly show a malignant tumor of the kidney when such a tumor is present. In other instances an obvious diagnosis from the picture or pyelogram may cause one to miss a tumor which is present.

Dr. Jenkinson will bear me out on these two cases, which I will mention briefly. About four years ago we saw a patient with a mild, spontaneous hematuria with no other symptoms. The patient was cystoscoped and pyelographed to find the source of the bleeding and on the pyelograms, which were very good, no lesion could be found except a hydronephrosis on the right side. The examination was repeated. Still no other lesion could be found and the patient was discharged from the hospital. About a year later he fell on the ice and was brought back into the hospital in more or less shock, with another hematuria following this fall. At this time he had ruptured a large hypernephroma of this kidney. We went back and looked at the roentgenograms which had been taken a year before. One calyx of this large hydronephrosis did look just a little bit frayed and a little bit fuzzy.

The other case that I want to mention is a case of a woman who came to us because she had some pus in her urine, occasionally a little hematuria, and a high temperature. Pyelograms and cystoscopic examination at that time revealed four or five large stones in the lower end of the megalo-ureter. This was also markedly affecting the ureter. A ureteronephrectomy was performed and a papillary tumor was demonstrated which could not be shown on the pyelograms. The patient subsequently died of metastases from this tumor. So we do not always want to think about the obvious. Sometimes one must look a lot closer and not be content with the obvious diagnosis from the roentgenograms.

When one reads the title of the third paper, "Ureteral Obstruction," most of us think immediately of ureteral strictures, and ureteral strictures are a matter of geography more or less. In the East the urologists see a great many more ureteral obstructions than we do and I think possibly that is due to the influence of urologists in those regions. One thing that Dr. Nichols brought out, and with which I agree heartily, is that a great many ureteral and renal lesions have predominant abdominal or gastrointestinal symptoms, and I think most of us should think more often of kidney and ureter pathology in vague abdominal symptoms.

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PYELOVENOUS BACKFLOW

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THE term "pyelovenous backflow" is generally used today to describe a fascinating phenomenon demonstrated occasionally on the retrograde pyelogram as an extravasation of opaque material into the venous system of the kidney. The phenomenon is not only fascinating but is important in the study of the circulation of the kidney, in the realization of the damage that may be done to the kidney during retrograde pyelography, and in the interpretation of pyelograms. Investigation of the phenomenon has thrown considerable light upon the venous, arterial, and lymphatic systems of the kidney. The extravasation of opaque medium and possibly infected urine into the blood stream may graphically explain reactions following retrograde pyelography which at times lead to a rise in temperature, sepsis, and possibly death. The characteristic findings of pyelovenous backflow on the roentgenogram have many times been erroneously interpreted by both urologists and roentgenologists as tuberculosis, tumors, and other forms of kidney extravasation and infection.

Voelcker and Lichtenberg[14] in 1906 were the first to demonstrate the practicability of outlining the urinary tract with opaque substances. The early use of silver salts as opaque substances and the subsequent demonstration of the ease with which these substances could be forced into the blood stream made retrograde pyelography somewhat of a hazardous procedure. The use of sodium iodide in subsequent years eliminated somewhat the reactions following pyelography but with the use of the halogenated organic substances of today such as hippuran, skiodan, and neoiopax, only rarely are difficulties encountered.[2] Renal pelves may be perforated by catheters, this being more easily done in children than in adults. The walls of the pelvis and ureter may be ruptured by pressure, particularly if weakened by infection, stones, or ulceration.[13]

Extravasation of opaque material into the kidney may be divided into four types: (1) pyelolymphatic backflow, (2) pyeloparenchymatous backflow, (3) pyelotubular backflow, and (4) pyelovenous backflow. Roentgenologists have a tendency to classify extravasations into only two types, pyelovenous backflow and the interstitial type. That pyelotubular and pyelolymphatic backflows also occur there is very little doubt and an effort should always be made to differentiate these various types.

The rarity of the demonstration of pyelolymphatic backflow is evidenced by the fact that up to 1937 only 15 cases had been reported, at which time Campbell and Seidler[6] added 2 additional cases. Roentgenologically pyelolymphatic backflow is recognized as irregular, tortuous, linear shadows 2 or 3 mm. in diameter extending from the kidney medially toward the spine. Occasionally these injected vessels appear to begin in the corticomedullary zone and extend medially past the pelvis toward the spine and then curve slightly downward. No marked pressure is required to produce pyelolymphatic backflow.

Chyluria is usually attributed to a blockage of the thoracic duct by the tropical parasite, *Filaria sanguinis hominis*, in the absence of an adequate collateral lymphatic circulation. Non-parasitic chyluria rarely occurs also. The exact mechanism whereby chyle reaches the urinary tract has never been satisfactorily explained; however, it is supposed that where there is an obstruction to the thoracic duct chyle passes retrogradely down the lym-

phatics that drain the kidney. Dilatation and stasis of the perirenal lymphatics occur which subsequently rupture into the urinary tract producing chyluria.[1] Some investigators have suggested the presence of lymph stomata in the pelvis but these have never been histologically or anatomically demonstrated. Hampton[8] in 1920 first reported a case of pyelolymphatic backflow with non-parasitic chyluria which was not clearly demonstrated on the pyelogram. Wood[15] in 1928 was the first to demonstrate clearly pyelolymphatic backflow on the pyelogram in a case of non-parasitic chyluria. In all cases of chyluria an attempt should be made to demonstrate pyelolymphatic backflow by retrograde pyelography and whenever pyelolymphatic backflow is demonstrated, chyluria should be suspected. Since chyluria may be intermittent, several specimens of urine should be examined.

Pyelotubular backflow has been a much discussed phenomenon. The findings of some workers seem to indicate with little doubt that this type of backflow actually occurs at times although their work has not always been confirmed. O'Conor[13] found that silver nitrate and mercurochrome could be forced up the collecting tubules to the glomeruli. Mason[10] in 1914 showed that substances could be made to ascend into the straight and convoluted tubules and into the glomeruli, this work being confirmed by Burns and Swartz[5] in 1918. Hinman and Lee-Brown[9] in 1924, using 2 per cent Berlin blue, were unable to demonstrate tubular reflux to any degree in fresh human kidneys even after using considerable pressure, while about two years later Bird and Moise[3] showed that India ink could be passed readily through the renal tubules to Bowman's capsule under pressures varying from 10 mm. of mercury to 100 mm. of mercury. They found little evidence of venous extravasation of the India ink, a finding somewhat opposed to the work of Hinman and Lee-Brown.

Since 1926 it has been found that pyelotubular backflow does occur at pressures usually used in clinical pyelography. The characteristic appearance of pyelotubular backflow is the short brush-like radiation extending outward into the medulla from the calyces for a distance of 5 or 6 mm. Occasionally pyelovenous and pyelotubular backflow occur simultaneously.

Pyeloparenchymatous backflow occurs following retrograde pyelography with pressures ordinarily used in filling the upper urinary tract. This interstitial type of extravasation is usually seen on the pyelogram as an irregular distribution of the opaque material in the medullary zone, about the major and minor calyces, about the pelvis, under the capsule, in the perirenal tissues, or along the upper portion of the ureter. This type of extravasation is more apt to occur with the use of the syringe method than with the gravity method. It may or may not be associated with pain in the kidney region and is frequently followed by bleeding from the involved side. Chills, fever, and even perinephric abscesses may follow this type of injury to the kidney.

In 1938 Narath[11] reported the first and only case of extrarenal extravasation from the renal pelvis during intravenous pyelography. This case showed no evidence of obstruction and the pelvis and calyces were never completely filled. There was no history of trauma to the kidneys. The occurrence of extravasation during intravenous pyelography and with such low intraureteral pressures during retrograde pyelography indicates the ease with which this type of accident may occur.

The subject of venous extravasation was brought to the attention of the medical profession by Hinman and Lee-Brown at the annual meeting of the Americal Medical Association in San Francisco in 1923 at which time they were awarded the Gold Medal for an exhibit showing this phenomenon. They chose to call this phenomenon "pyelovenous backflow." These workers found, by injecting postmortem kidney specimens of humans, sheep, dogs,

and rabbits, using moderate intrapelvic pressures, that the pelvic contents passed back into the renal veins. The pressures used were always below maximal secretory pressures and gross and microscopic studies showed no evidence of local rupture. By using anesthetized sheep and dogs with the ureters exposed, they were able to demonstrate roentgenographically and by sections pyelovenous backflow following injection with sodium iodide solution and 2 per cent Berlin blue solution at pressures as low as 20 mm. of mercury.

In order to appreciate the problem of pyelovenous backflow one must have some knowledge of the vascular system of the kidney. The renal artery ordinarily possesses three branches which pass up into the hilum and ramify through the interstices forming interlobar and arcuate arteries. From the arcuate arteries fine radial branches pass at right angles to the renal surface to supply the cortex. The arterial supply is an end one, there being no anastomosis.

The fine radially fashioned interlobular veins begin in the cortex and pass inward forming anastomosing arcades at the corticomedullary zone. From these arcades spring interlobar veins which pass downward toward the hilum next to the wall of the calyces and frequently in contact with the mucosa of the calyces. In the region of the fornices of the calyces the interlobar veins arch around the pyramids and it is at this point that most investigators feel that pyelovenous backflow first begins. The interlobar veins collect into usually three branches of the renal vein.

The mechanism of pyelovenous backflow has not, even up to today, been satisfactorily explained. Levin[1] in 1903 thought that possibly there existed natural communications between the renal pelvis and the venous system. Hinman and Lee-Brown in 1924 felt that distention of the calyces produced a spreading of the fornices between the calyces and the papillae resulting in minute ruptures into the adjacent rich venous plexus. Bird and Moise in 1926 suggested that the reflux first occurred up the collecting tubules and then ruptured into the adjacent interlobular veins. This explanation seemed to be somewhat disproved in 1927 by Brown[4] who showed that the hypodermic injection of India ink into the cortex of fresh kidneys resulted in the filling of the venous capillary system with very little being found in the tubules. This fact seemed to show that the venules were much more fragile and subject to rupture than the tubules. Fuchs[7] in 1930 believed the extravasation occurred in a perivenous fashion before there was a final rupture into the veins.

It is quite surprising to see pyelovenous backflow, as well as the other types of renal and perirenal extravasation, following the use of such low pressures. Scott[12] in 1933 in connection with the study of effects on the pyelogram of various pressures found that great pressure of the injected medium does not enlarge the pyelographic shadow beyond that of a normally filled one. This would seem to eliminate the impression that apparent dilatation of the upper urinary tract is due at times to overdistention and not to hydronephrosis. Scott also found that 25 per cent of 162 injected postmortem specimens, using 30 mm. of mercury pressure, showed pyelovenous backflow and that shape and disease of the pelvis played no part in the occurrence of this phenomenon.

In the pyelogram pyelovenous backflow is seen as cone-shaped funnels beginning just beyond the minor calyces. In the corticomedullary zone, arcades of anastomosing veins may be seen from which extend into the cortex radiations of opaque material. Pyelotubular backflow is always in the form of short brush-like tufts extending out from the tips of the calyces. Arcades and cortical radiations are never seen in pyelotubular backflow. It also must be remembered that both pyelotubular and pyelovenous backflow may occur simultaneously.

The following case is presented for it represents a phase of pyelovenous backflow

Fig. 1. A right retrograde pyelogram with an opaque catheter in the right ureter shows irregularity of the calyces and extravasation of the opaque medium indicative of pyelovenous backflow. The areas of increased density in the right side of the abdomen are extra-ureteral.

occurring in the living human that has not been described before.

White, unmarried female, aged fifty-eight. Admitted to the University of Maryland Hospital January 5, 1939 complaining of soreness in the right lumbar region and pain in the right upper quadrant of the abdomen. The patient complained of nocturia of three times for many years. No hematuria, pyuria, burning, tenesmus, or frequency present. The patient had been seen in a private office a few days before admission and had had a plain film of the kidneys, ureters, and bladder. On the film two areas of increased density were seen on the right which suggested ureteral calculi.

The physical examination showed moderate obesity,a blood pressure of 192/112,and tenderness over the 12th right rib.

Blood and urinary studies were normal. Phenolsulphonphthalein excretion was 90 per cent in two hours. Non-protein nitrogen in the blood was 27 mg. per 100 cc. of blood. Wassermann reaction negative.

Cystoscopy showed the urethra normal; bladder was normal. Moderate trigonitis present. Right ureter catheterized easily with a No. 5 catheter. A No. 5 catheter could not be passed up the left ureter. A plain film with the catheter in the right ureter showed the areas of increased density not in relation to the catheter. With a syringe 18 cc. of skiodan was injected in the right pelvis. The pyelogram showed the areas of increased density to be not in the ureter. Considerable pyelovenous backflow had occurred. The pelvis was refilled about twenty minutes later and a film was made. Less pyelovenous backflow occurred on the right but a pyelogram of the left kidney was also seen,

Fig. 2. The right kidney pelvis was reinjected. The film was made about twenty minutes after the first injection as indicated in Figure 1. The extravasated dye has disappeared. The calyces appear sharper in outline. At this time a pyelogram is noted on the opposite side, evidently due to excretion of the dye that had been extravasated into the venous system on the right side at the time of the first pyelogram.

evidently due to excretion of the extravasated dye on the left. No bleeding occurred after the pyelovenous backflow and there was no post-cystoscopic reaction.

The only analogous phenomenon found in the literature occurred in the experimental work of Hinman and Lee-Brown in 1924. These workers exposed the ureters of an anesthetized sheep, filled one pelvis with a solution of phenolsulphonphthalein at 40 mm. of mercury pressure and shortly phenolsulphonphthalein appeared in the urine from the opposite kidney. Subsequent examination of the kidneys showed no rupture or extravasations.

The appearance of dye in the opposite kidney shows without doubt that pyelovenous backflow actually occurred. This graphic demonstration might be more often observed if additional films were routinely made ten or fifteen minutes after discovery of pyelovenous backflow.

SUMMARY

1. The four types of kidney extravasation are reviewed and their differential characteristics are pointed out.

2. The case of pyelovenous backflow presented adds new evidence that venous extravasation occurs.

The privilege of reporting this case, granted by Dr. J. Mason Hundley, Professor of Gynecology, University of Maryland, Baltimore, Maryland, is acknowledged.

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LATERAL PYELOGRAPHY*

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THE lateral pyelogram is an aid to the study of pathologic behavior. It is not recommended as a routine examination but it is frequently indicated and sometimes necessary. We will not attempt to establish diagnostic dogma but will discuss briefly our experiences with lateral pyelography during the past five years.

TECHNIQUE

The lateral pyelogram is made on the regular cystoscopic table. The patient must be in an exact lateral position with the questionable side next to the film. The side uppermost is subject to considerable distortion. The ureter and/or kidney is refilled, depending on whether a ureteropyelogram or pyelogram is desired, and roentgenographed with the shortest possible exposure. The roentgenogram should visualize the usual quantity of pyelographic medium or leaded catheter in the ureter and kidney. Occasionally, in large individuals, an increase in concentration of the pyelographic medium permits better visualization. The catheter may be left in the opposite ureter when for some reason it is advisable to do so. The best results are obtained by retrograde technique, but in those pathologic processes accompanied by stasis, lateral intravenous urography can be done quite satisfactorily (Fig. 3*A* and *B*).

FIG. 1. Position of kidney and ureter normal for this individual. Ureter slightly forward at level of lumbosacral joint because of catheter tension.

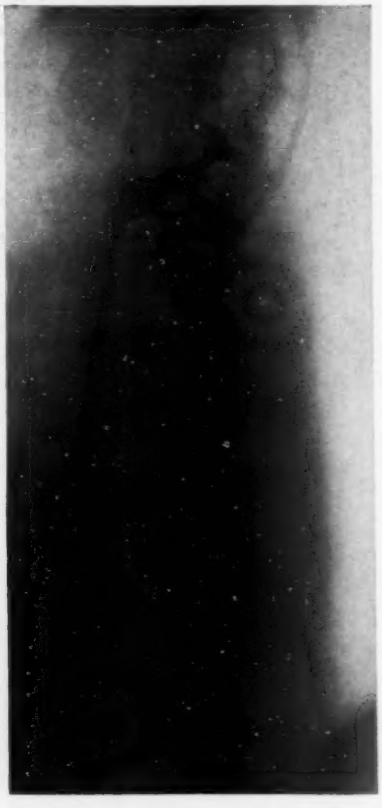

FIG. 2. Horizontal rotation with calyces directed posteriorly. Position of ureter and kidney otherwise normal. Constriction below ureteropelvic junction was shown on routine pyelogram. No surgery.

* Read at the Thirty-ninth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 20–23, 1938.

NORMAL LATERAL PYELOGRAM

We usually, but with certain modification, use Mertz's criteria of the normal lateral pyelogram. The shadow of the pelvis is usually superimposed on that of the second lumbar vertebra, but sometimes on part of the first and second, or second and third lumbar vertebrae. The long axis of the renal pelvis and the spine correspond. The superior and inferior calyces extend up and down respectively (Fig. 1), but if there is some rotation of the kidney on its long axis, the significance of which is not yet entirely understood, the calyces may point backward towards the spinous processes, or be visualized through the pelvis (Fig. 2). The ureter descends in a smooth convex curve anteriorly behind the shadow of the vertebral bodies until it reaches the inferior margin of the fourth lumbar where it becomes anterior and passes downward just anterior to the fifth lumbar and the lumbosacral joint, then becomes slightly convex posteriorly to deep in the pelvis where it again comes forward to enter the bladder (Figs. 1 and 2). The anterior surface of the ureter in relation to the peritoneum is fairly constant. Normal variables must be learned by experience.

ESSENTIAL INFORMATION

The lateral pyelogram should establish the type and the degree of rotation of the kidney, and the anteroposterior position of the kidney and the ureter. We use Mertz's terminology of vertical and horizontal rotation, that is, rotation on the short and long axis respectively. Combination of types and degrees of rotation and displacement vary with different lesions and constitute the essential basis of diagnosis from lateral pyelography, but this information must be correlated with that obtained from the routine pyelogram, and pathologic behavior. The most significant combination is that of vertical rotation and displacement.

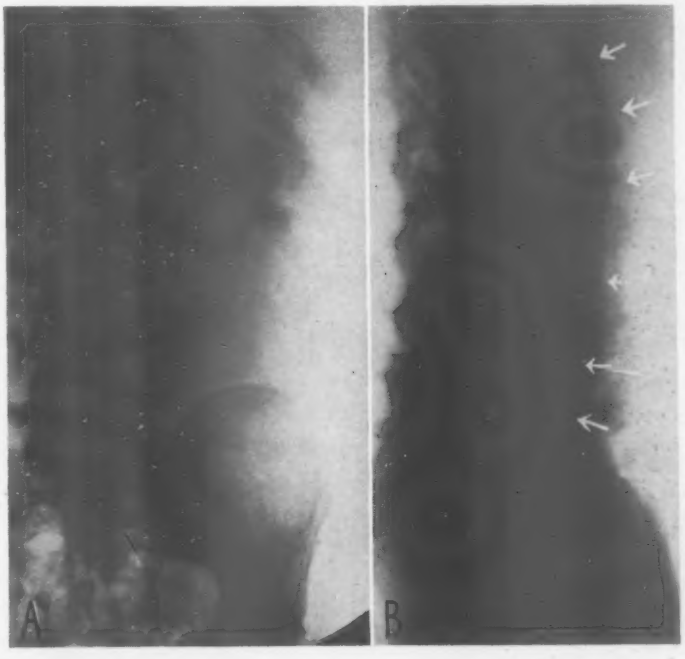

Fig. 3. *A*, sixty minute urogram. Kidney displaced laterally, more at upper pole. A dynamic type of hydronephrosis and hydroureter. Lumbar scoliosis with concavity to left, increased left-sided density, psoas muscle poorly visualized. Pathologic behavior of infection. *B*, anterior displacement of kidney and ureter. Slight vertical and horizontal rotation. Diagnosis of large perinephric abscess with generalized infection of retroperitoneal space made. Surgery: incision and drainage; 1,000 cc. pus obtained.

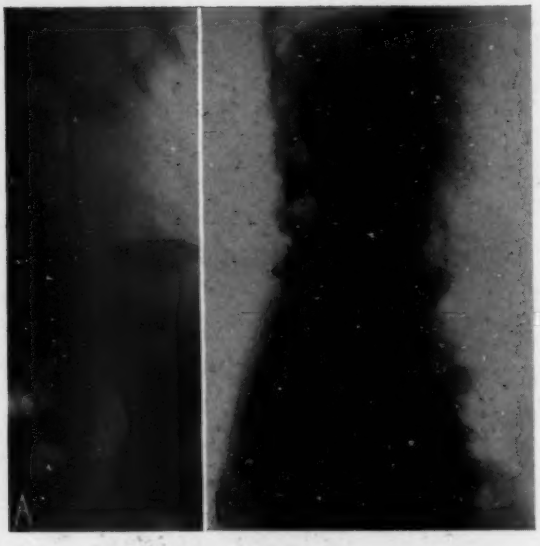

FIG. 4. *A*, large dense kidney, small hydronephrosis, moderately dilated ureter, apparently deformed lower calyces, lumbar scoliosis, concavity to left, increased left-sided tissue density becoming lateral and convex at brim of the pelvis. *B*, anterior displacement of the kidney and ureter, vertical rotation, lower pole forward. Perinephric abscess located inferiorly.

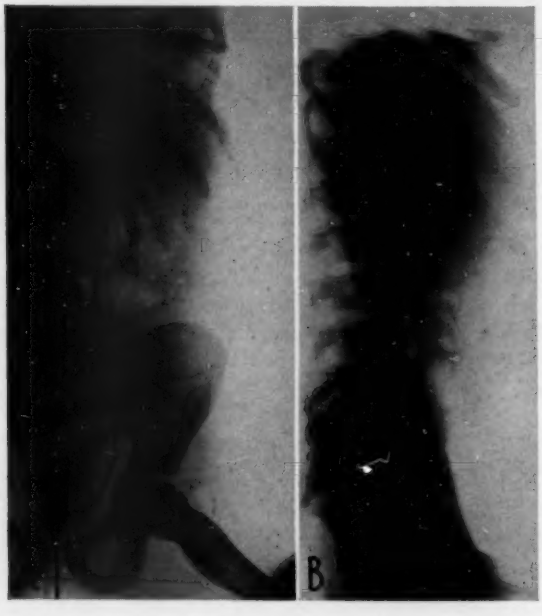

FIG. 5. *A*, slight horizontal rotation. Spasm and irregular contraction of upper end of ureter. Small amount of gas in small bowel. *B*, slight anterior displacement of kidney and ureter, rotation chiefly horizontal. Roentgen diagnosis was perinephric infection but in addition there was a subcapsular abscess which was not diagnosed from roentgenogram.

LESIONS SUBJECT TO STUDY

We have found the information obtained helpful and at times conclusive in the diagnosis of the following lesions: renal neoplasms and cysts, perinephric abscess, primary retroperitoneal tumors, retroperitoneal infections, tumors arising from organs adjacent to kidney, retroperitoneal

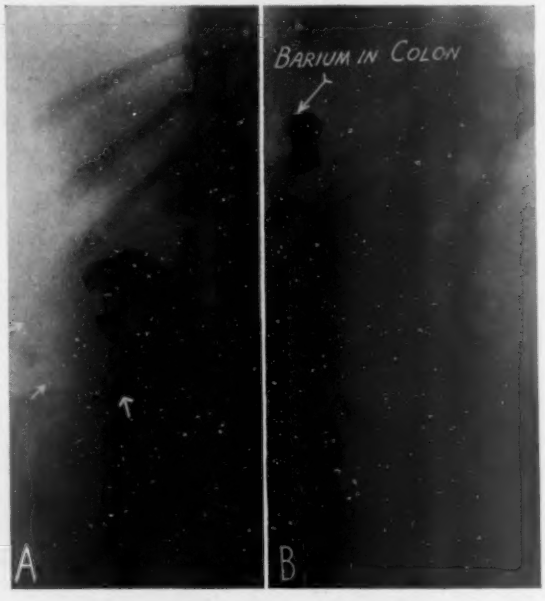

FIG. 6. *A*, enlarged lower renal pole (due to rotation). Questionable deformity of calyces. Clinical history suggested carcinoma of colon. Anteroposterior pyelograms showed what appeared to be a tumor of the kidney. *B*, kidney pelvis organically normal. Anterior displacement of kidney and ureter, vertical (short axis) and horizontal (long axis) rotation. Diagnosis: retroperitoneal tumor, probably sarcoma, slight mechanical hydronephrosis. Surgery and biopsy: chronic indurated perinephric abscess, normal kidney.

metastatic malignant growths, congenital and acquired abnormalities of the kidney and ureter, and in a large group of miscellaneous conditions encountered from time to time in the investigation of the urinary tract.

Perinephric Abscess. Since the retroperitoneal space is potential an increase in solid or fluid medium from inflammation manifests itself by extension along natural planes of tissue cleavage and by displacement of organs in the direction of least resistance which is usually forward and

downward, modified occasionally by the difference in the relationship of the right and the left kidney.

Perinephric abscess causes predominantly anterior displacement of the kidney and the ureter, but this is associated with variable degrees of vertical and horizontal rotation (Figs. 3, 4 and 5). The amount of displacement depends upon the extent of the infiltration and the degree of suppuration (Fig. 3*A* and *B*), and the direction of rotation, the probable location of suppuration (Fig. 4*A* and *B*). When these dynamic signs are correlated with acute pathologic behavior, the diagnosis becomes relatively simple. A chronic indurated perinephric abscess without the evidence of acute pathologic behavior may be quite difficult, if not impossible, to differentiate from a retroperitoneal sarcoma (Fig. 6*A* and *B*). This simple procedure should decrease the number of explorations for acute abdomen, since perinephric abscess does cause considerable peritoneal irritation with symptoms easily mistaken for an intra-abdominal condition.

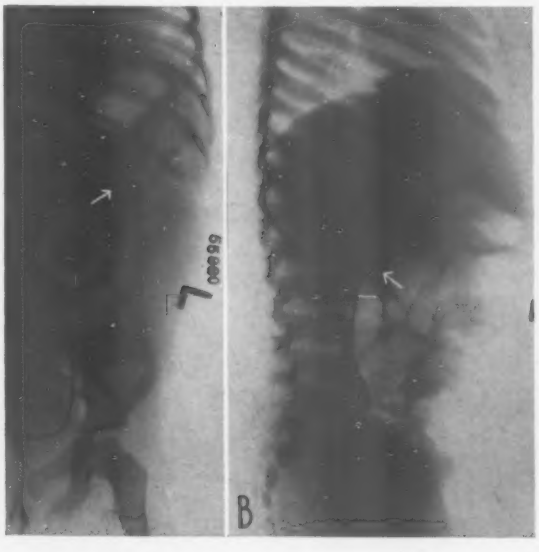

Fig. 7. *A*, horizontal rotation, outward displacement of the lower pole, filling defect in pelvis at tip of catheter. Information not conclusive. *B*, lateral roentgenogram shows invasion of pelvis. Working diagnosis of Wilms' tumor. Tumor regressed in size, and there was return of function following irradiation. (Courtesy of Dr. H. O. Mertz.)

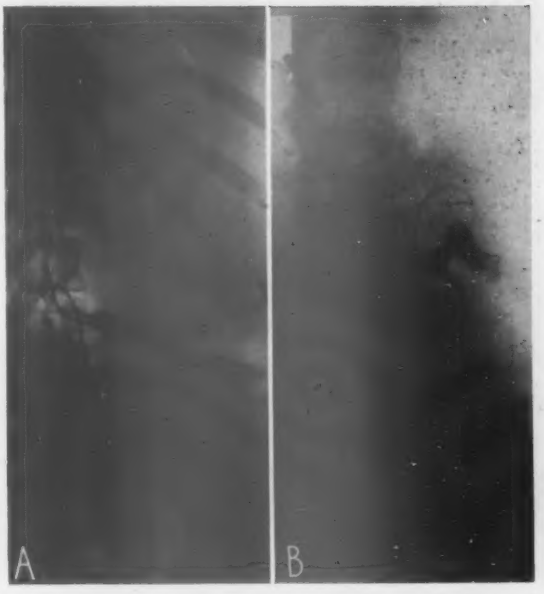

Fig. 8. *A*, large upper quadrant tumor. Kidney displaced to pelvic brim. Pelvis rotated. *B*, extreme vertical rotation, no appreciable anterior displacement, kidney pelvis intact. Sarcoma tail of pancreas. (Courtesy of Dr. H. O. Mertz.)

Tumors of the Kidney. The greater number of cortical neoplasms can be detected from the routine pyelogram. Occasionally, the lateral pyelogram will give the only conclusive evidence of a renal neoplasm (Fig. 7*A* and *B*), permit the differentiation of retroperitoneal tumors displacing the kidney (Fig. 8*A* and *B*), or prevent the diagnosis of tumor because of a vertically rotated kidney (Fig. 6*A* and *B*).

Cortical neoplasms cause predominantly vertical rotation, variable degrees of horizontal rotation, and little if any, more frequently no anterior displacement, of the kidney or the ureter, Mertz (Fig. 9*B*). If there is appreciable anterior displacement of the kidney and a localized segment of the ureter with evidence of an intrarenal malignant growth, the tumor has probably invaded perinephric structures and the choice between surgery and irradiation should be seriously considered because the case is probably inoperable (Fig. 10*A* and *B*). We suggest that the lateral pyelogram be employed in all cases clinically

or roentgenologically suspected of malignant growth.

Cysts. Large solitary cysts of the kidney cause considerable vertical and horizontal rotation without a comparable degree of anterior displacement, even when the cyst is huge (Figs. 11, 12 and 13), and most frequently there is no appreciable displacement (Figs. 12 and 13). Other criteria for cysts must be employed. In our experience cysts cause less compression deformity than a malignant tumor of comparable size, rarely distort the pelvis unless there is associated infection, and often appear as an accessory rather than an incorporated mass because of the difference in the genesis of the lesion. There is practically always a mechanical hydronephrosis which may be general or partial, due to chronic compensation which is more frequently not present in malignant neoplasms because of the more rapid growth of the latter. A great effort should be made to differentiate between small serous cysts and small neoplasms because the solitary cyst often causes no symptoms and a useless operation with clinical failure may be avoided. If there is an element of doubt the patient should receive the benefit of it. The differential diagnosis is particularly difficult when the small cyst involves the upper pole, because the law of probability favors a malignant neoplasm.

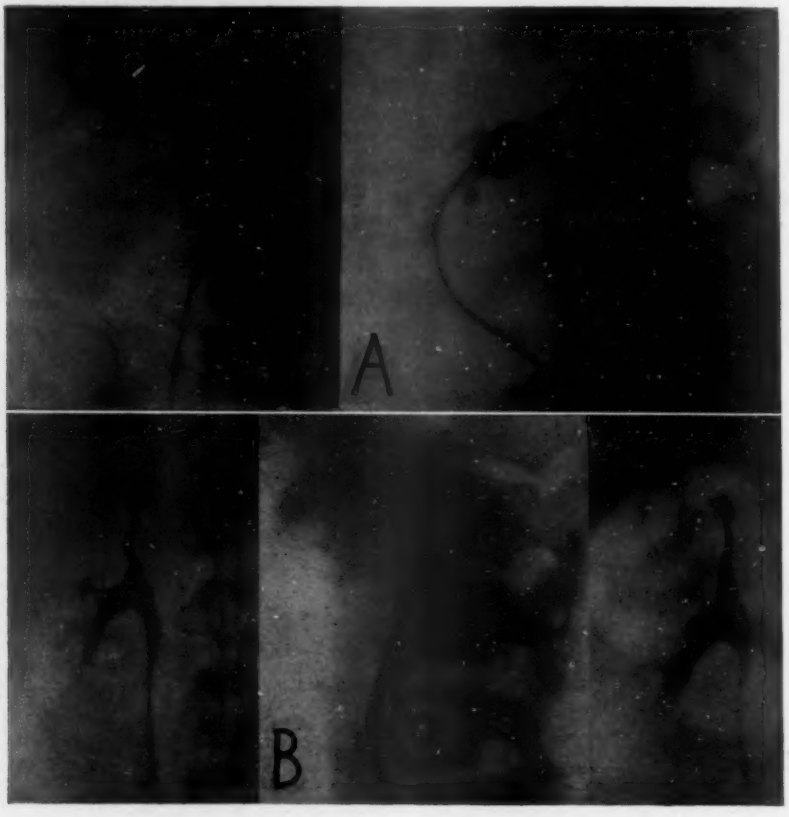

FIG. 9. *A*, anteroposterior and lateral pyelograms in a case of retroperitoneal sarcoma. There is considerable anterior displacement of the kidney and ureter and marked horizontal and vertical rotation of the kidney. *B*, the two small figures to the left show influence of hypernephroma. Vertical rotation of slight degree and compression of kidney pelvis. The single figure to extreme right, reading from left to right, shows increased size of the hypernephroma.

Retroperitoneal Tumors. These include

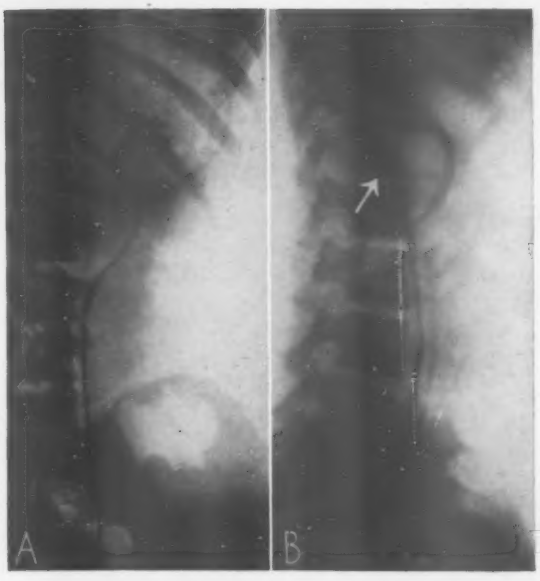

Fig. 10. *A*, calyces tuffed superiorly. Nonopaque filling defect in pelvis. Lateral displacement of kidney and upper end of ureter. Tumor of abnormally developed kidney suggested. Can the diagnosis be more specific? *B*, vertical and horizontal rotation; anterior displacement of kidney and upper end of ureter, lower half of kidney pelvis hydronephrotic and displaced upward; pathologic behavior of a malignant condition. Diagnosis of perinephric extension confirmed by surgery. Was not removable. No biopsy.

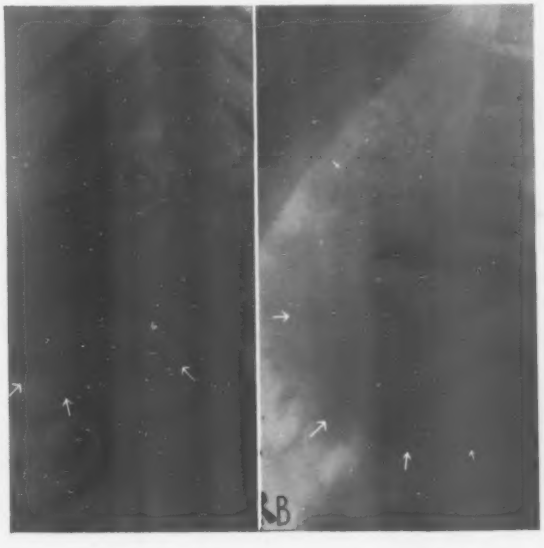

Fig. 12. *A*, large tumor lower pole of right kidney. Pelvis displaced upward and rotated. *B*, 90 degree vertical rotation lower calyces anteriorly. Hydronephrosis of cephalic calyces. No anterior displacement. Solitary cyst.

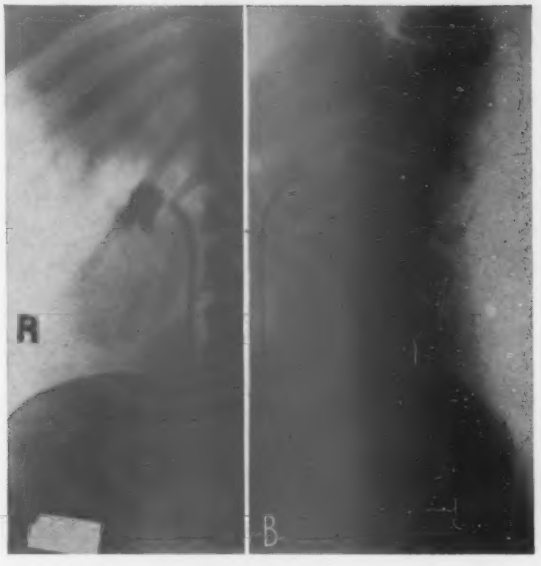

Fig. 11. *A*, large, slightly irregular tumor lower pole right kidney. Pelvis pushed up. Actual condition of pelvis not demonstrated. *B*, considerable vertical rotation of kidney, lower half of kidney pelvis compressed, but pelvis otherwise intact. No anterior displacement. Solitary cyst. (Courtesy of Dr. H. O. Mertz.)

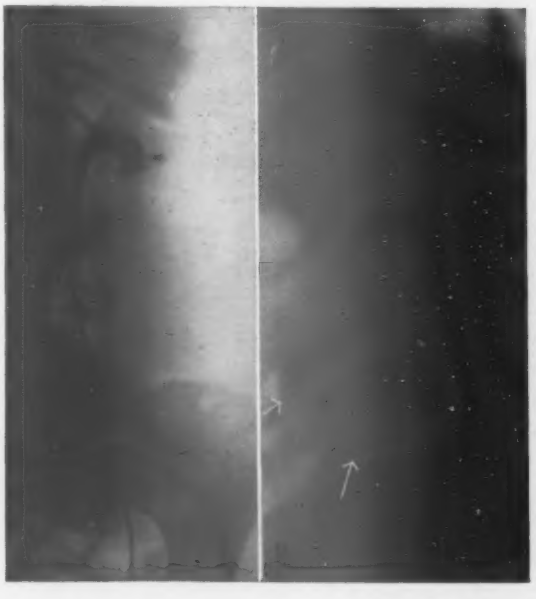

Fig. 13. *A*, large tumor lower pole of left kidney displacing pelvis upward. Condition of pelvis not demonstrated. *B*, pelvis intact except for mild compression; 90 degree vertical rotation. No appreciable anterior displacement comparable to size of mass. Solitary cyst. (Courtesy of Dr. H. O. Mertz.)

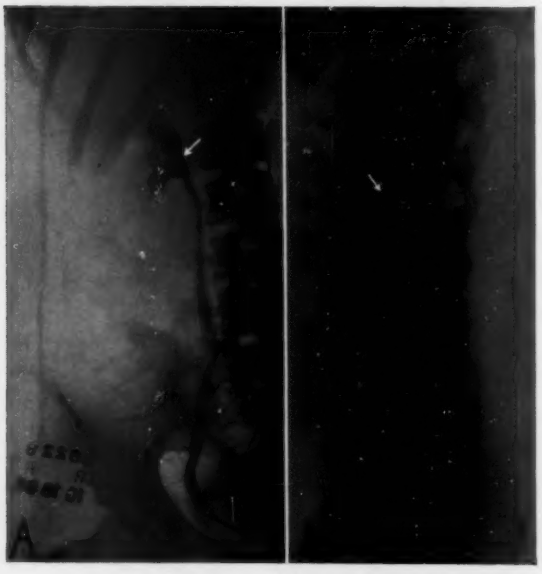

FIG. 14. *A*, appendectomy without relief. Urography: hydronephrosis from ureteropelvic junction obstruction. Retrograde: ureteropelvic junction obstruction evident but lesion is not demonstrated. *B*, lesion and sacculated hydronephrosis shown. Diagnosis of aberrant vessel. Is to return for surgery.

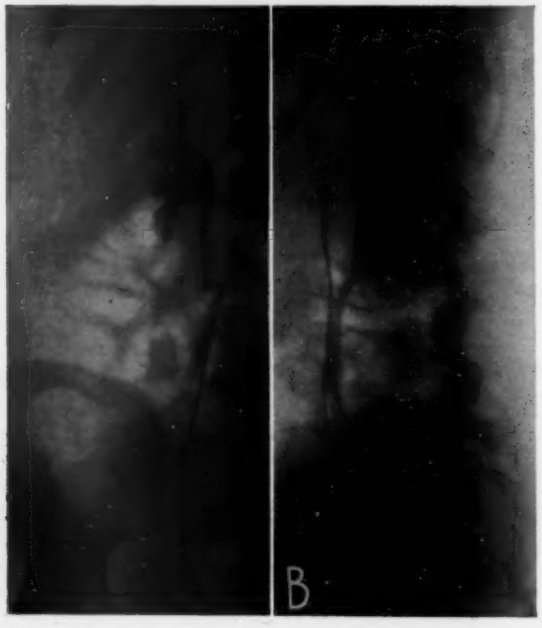

FIG. 15. *A*, anteroposterior roentgenogram fails to demonstrate exact type of ureteropelvic junction lesion but suggests aberrant vessel. Kinking at tip of catheter due to catheter. *B*, lateral roentgenogram shows unquestionable deformity of aberrant vessel and the hydronephrosis to be larger, and sacculated. The kidney is a little posterior. A short pedicle was present. The possibility of a posterior position due to short pedicle will be studied in future cases.

both the true retroperitoneal sarcoma, and tumors originating from retroperitoneal organs other than kidney, particularly the tail of the pancreas. Primary retroperitoneal tumors cause considerable anterior displacement which is always associated with a considerable degree of horizontal

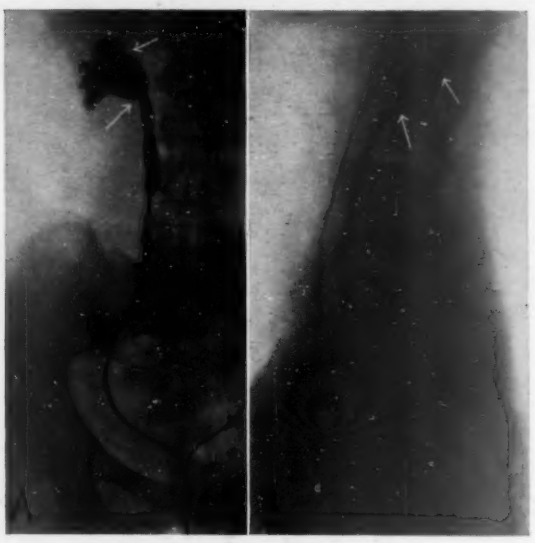

FIG. 16. *A*, stone demonstrated in pelvis by roentgenogram of the kidney, ureter and bladder included in medium and not visible on pyelogram. General, with localized increased hydronephrosis of upper calyx. Cause not clearly seen. *B*, stricture of cephalic infundibulum causing increased partial hydronephrosis. Ureteropelvic junction obstruction causing general hydronephrosis. Evidence of infection which is more advanced in obstructed calyx. No surgery.

and vertical rotation (Figs. 8*A* and *B* and 9*A*), thus tending to differentiate them from perinephric abscess which causes predominantly anterior displacement of the kidney and ureter, and from primary renal tumors which cause predominantly vertical and horizontal rotation of the kidney without displacement or appreciable displacement of the kidney and the ureter. If a retroperitoneal lesion is demonstrated

and does not conform to these criteria one must carefully consider other possible origin with the probable result of the physical force of the lesion. This will at times determine its origin if not the actual nature of the tumor (Fig. 8*A* and *B*). The

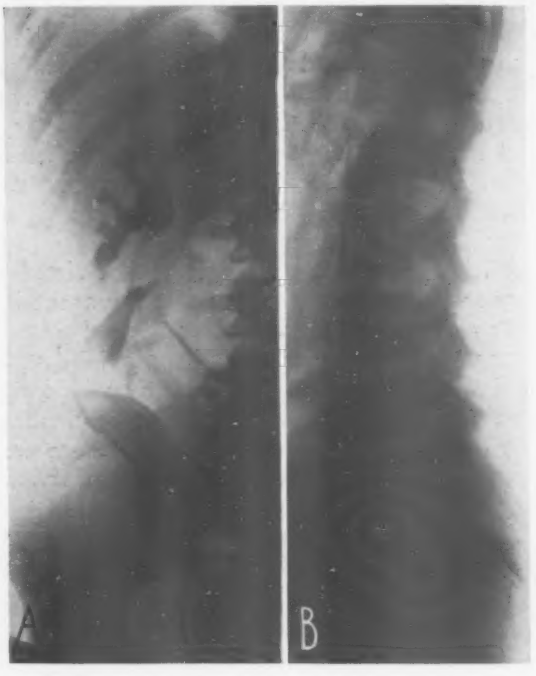

Fig. 17. *A*, crossed dystopia. Catheterization of right ureteral orifice failed to give relief. Catheterization of left ureteral orifice with relief. Urogram sixty minutes. Left catheter for drainage. Note correct point of direction of pelves and point of crossed kidney inferiorly. *B*, kidneys and ureters in relatively normal anteroposterior position.

lateral pyelogram thus emphasizes the importance of physical properties in urological diagnosis.

Miscellaneous. This includes too great a number of abnormal conditions to be discussed here. A good rule to follow is to make a lateral pyelogram when the routine pyelogram leaves one in doubt as to the probable significance of some aberration from the average normal. Congenital (Figs. 14 and 15) and acquired lesions (Fig. 16*A* and *B*) at the ureteropelvic junction, vague causes of partial and complete hydronephrosis (Fig. 15*A* and *B*), unusual appearing pelves (Figs. 4, 6, 7, 10, 11, 12 and 13), anomalies of development which might lead to clinical confusion (Fig. 17*A* and *B*), and calcifications anterior or posterior to the kidney which may appear to be in the kidney pelvis because of superimposition, and differentiation between intra-abdominal and retroperitoneal masses, etc., all lend themselves well to study by lateral pyelography.

SUMMARY

The lateral pyelogram has a wide range of usefulness. The technique is simple and does not appreciably delay the urologist or add to the discomfort of the patient. The normal variable is much less than in the average system which makes it relatively easy to detect the pathologic. It permits convincing localization between intra-abdominal and retroperitoneal tumors and in the differentiation of retroperitoneal lesions themselves, and can be used to advantage in the roentgenological investigation of all urinary tract problems. Elective lateral pyelography is of as much value as the lateralization of any other organ or system of organs and should be placed on an equal plane.

We wish to express our appreciation to the staff of the Kentucky Baptist Hospital for making this paper possible, and particularly to Drs. J. R. Stites and J. Andrew Bowen who have been more than generous in their helpful advice and in permitting the use of their urological material, and to Dr. H. O. Mertz, Indianapolis, Indiana, who has kindly contributed several illustrations.

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DISCUSSION

Dr. Bernard H. Nichols, Cleveland, Ohio. It was a pleasure to be asked to discuss

this paper because this is a subject which has apparently been somewhat neglected. As has been said, Dr. Mertz's paper on "Lateral Pyelography" showed the value and described definitely most of the occasions in which this method of examination may be utilized to advantage.

We have been much interested in lateral pyelography, particularly in the diagnosis and location of suspicious shadows in the region of the kidneys. Quite often it has been our experience that dense shadows which appeared to be calculi lost in the pyelographic medium on an anteroposterior exposure were, to our chagrin after making a pyelogram, shadows either posterior or anterior to the kidney. Therefore, we now almost routinely do a lateral pyelogram where renal calculi are suspected if they are not definitely identified by either a pyelogram or an excretory urogram.

We have also found this procedure to be a most valuable adjunct to our present methods of examination of patients suspected of having a perinephritic abscess. Dr Menville, in his paper on "Perinephritic Abscesses" published in the June issue of the *Journal of the American Medical Association*, described the importance of lateral pyelography as an aid in the diagnosis of these lesions. Dr. Shiflett, today, has again called attention to the value of this procedure. It has been particularly valuable in cases of a well established abscess as, by the presence of the collection of pus at the lower pole of the kidney—usually the medial side—the kidney is displaced forward, together with the ureter, which produces a somewhat crescent-shaped deformity. There are few things, except possibly a smooth, symmetrical tumor either of the lower pole of the kidney or a perirenal tumor and possibly an aneurysm of the abdominal aorta, which might produce such a deformity. However, with the clinical history and the other known findings which we have depended upon so long, it is not difficult in most instances to correctly establish the diagnosis of a perinephritic abscess.

With the present speculations that circulatory renal disturbance is a causative agent in the production of hypertension, lateral pyelograms, we feel, are of importance in determining the torsion of the kidney on its long axis. This may be a definite factor in circulatory disturbance if Dr. Goldblatt's findings are true, in which case this type of examination may become very valuable.

As the speaker has shown so well, there are many other uses for this type of examination and one in particular is the demonstration of a stricture of the upper end of the ureter in the presence of a redundancy.

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CALCULUS IN A URACHUS

REPORT OF A CASE WITH ENURESIS*

By GEORGE M. WYATT, M.D., *and* THOMAS H. LANMAN, M.D.
BOSTON, MASSACHUSETTS

THE finding of a calculus in a urachus is unusual. A survey of the literature reveals only one reported case.[1] In that instance, the stone was of considerable size, operation was refused, and the patient died of uremia.

The case reported below is of particular significance in that it again calls attention to the importance of giving the most careful consideration to the symptom of enuresis in a child. A variety of organic lesions in the urinary tract may be responsible for urinary incontinence in early life.[2] Particularly important are certain congenital anomalies, among which are posterior urethral valves, ectopic ureters, anomalies of the spine, and lesions of the central nervous system.

Every effort must be made to exclude organic lesions before treating any patient with urinary incontinence as a mental or emotional problem.

REPORT OF CASE

The patient was a white male, aged seven, who came under our observation because of apparent inability to acquire normal urinary control. Bed wetting was constant. Control during the day was not normal, but on close questioning it was suggested that the lack of control was an urgency with incontinence rather than true incontinence.

His birth history and past history were entirely normal. He had had no serious illnesses. His parents were highly intelligent and had sought advice from several physicians regarding the boy's urinary difficulties, which were now causing considerable trouble, particularly because of comments by his school- and playmates. Repeated urinary analyses had failed to show any evidence of infection. General physical examination revealed no abnormalities.

Roentgenograms were taken of the lumbosacral spine in an effort to exclude a congenital anomaly of the spine as a causative factor in the enuresis. The calculus was noted on these films and described as being rather far anterior, but still within the limits of the bladder area. Intravenous pyelography was done to visualize the urinary tract and determine the exact location of the calculus in relation to the bladder (Fig. 1, *A* and *B*). The shadow of the calculus was seen to project anteriorly from the bladder wall in the region of the urachus. A diagnosis of stone in the lower end of the urachus was made and operation advised.

Operation. A midline suprapubic incision was made from just below the umbilicus to the symphysis. The rectus muscles were pulled laterally, the prevesical space entered, and the bladder freed. The peritoneum was stripped upward and on approaching the dome of the bladder, the fibrous cord of the urachus was seen. This cord-like structure fanned out as it entered the bladder wall. Incision was made just below it into the bladder and on exploring with the finger and everting the mucous membrane of the bladder a pedunculated mass the size of a large pea was encountered. This mass had its base in the bladder wall (Fig. 2). It was excised, and about 2 cm. of the tract of the urachus was excised with it. On cutting across this fibrous tract about 2 cm. distal to the bladder no lumen could be identified. The tract was tied at this point with catgut. A catheter was placed in the bladder. The bladder wall was closed about it in the usual manner. A drain was placed in the prevesical space and the skin and fascia closed with silk.

The pathologist's report is as follows:

Gross Description. The specimen consists of two pieces of tissue, one measuring 1.3×1.3×0.6 cm. in its greatest diameter, the other 1.1×0.5×0.3 cm. The first piece is roughly pearshaped, and reveals a normal appearing whitish-gray mucosal surface, except on one side where a recent cut surface of reddish color is noted. On palpation a firm stone-like mass is found in the center of this piece. The second specimen exhibits on one side a mucosal surface similar to that described above, while the other surfaces are of a reddish-yellow color. This

* From the Departments of Roentgenology and Surgery of the Infants' Hospital, and the Children's Hospital, Boston, Massachusetts.

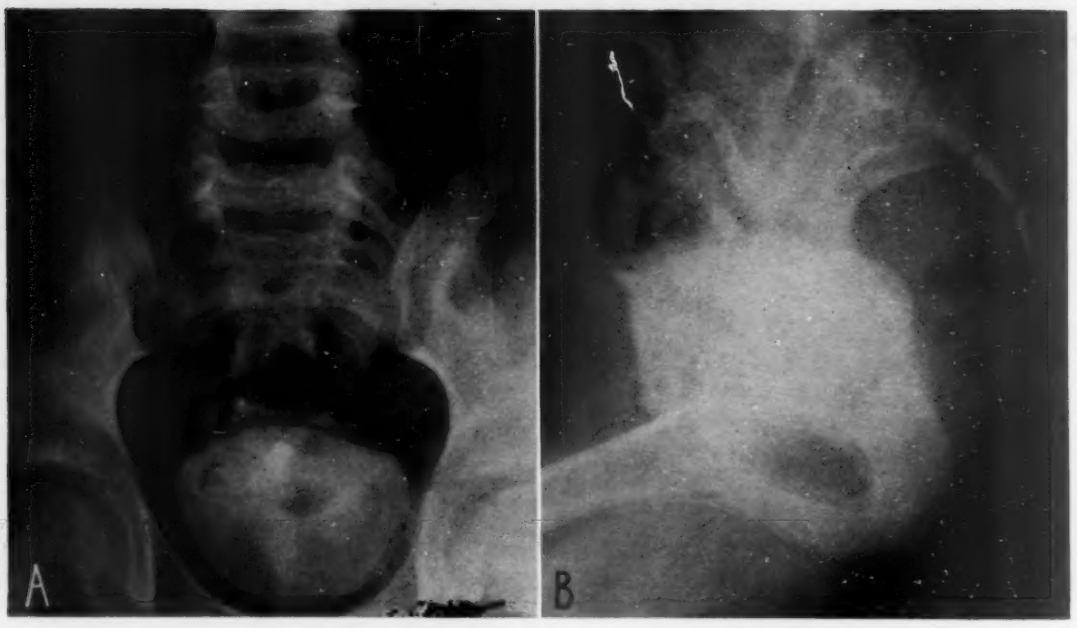

FIG. 1. *A*, anteroposterior film of the urinary tract following intravenous injection of 17 cc. of 35 per cent diodrast shows the shadow of the calculus to lie within the margins of the dye-filled bladder. *B*, in the lateral view, the shadow of the calculus projects anteriorly from the margin of the bladder in the region of the urachus.

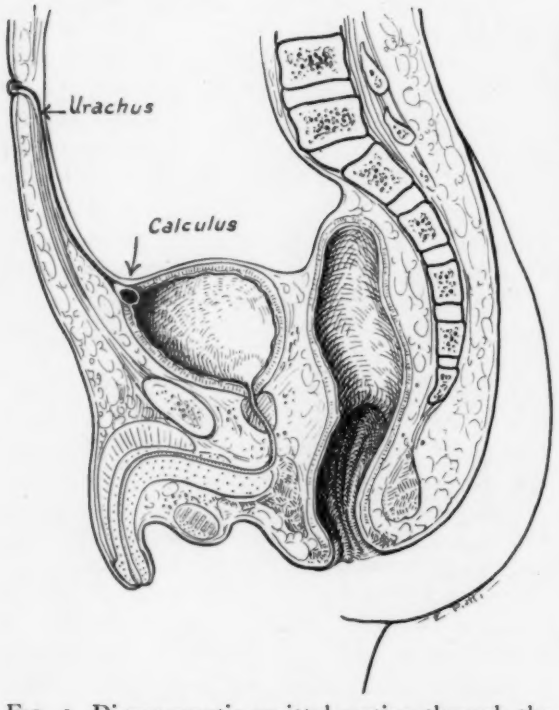

FIG. 2. Diagrammatic sagittal section through the lower abdomen shows the relationship of the urachal remnant and the calculus to the abdominal wall and bladder.

FIG. 3. Photomicrograph of a section through the calculus. *A*, area of calcification; *B*, bone; *C*, connective tissue.

piece is of tendon-like consistency. No lumen is found in the specimen. Representative sections are placed in Zenker's fluid and 10 per cent formalin.

Microscopic. Three sections stained with eosin, methylene blue were examined. The sections show connective tissue which in one section is covered by a lining of transitional epithelium. The connective tissue immediately below this transitional epithelium is loose and contains numerous congested vessels and numerous small areas of recent hemorrhage. In another section the connective tissue is of a more dense collagenous character, and intermingled with numerous bundles of smooth muscle fibers. The third section shows the connective tissue which surrounds and includes large deposits of calcium and some newly formed bone.

This area of calcification, which is completely surrounded by dense connective tissue, consists of numerous small and large masses of dense basic staining material, often arranged in circular masses. Scattered throughout the area of calcification are small masses exhibiting definite bone formation. Nuclear structures stain poorly and osteoblastic activity is not marked (Fig. 3).

Diagnosis. Calcification and ossification of remnant of urachal cyst.

The patient had an uninterrupted convalescence and was discharged on the sixteenth postoperative day, at which time the suprapubic wound had healed, and he was voiding normally through the urethra.

It is gratifying to report that since operation the boy's control during the day became practically normal within a very short time. The night bed wetting was a little harder to overcome, but now, four months after operation, the parents report that he has no trouble except occasionally when he is overtired. These episodes are becoming less and less frequent.

DISCUSSION

It is interesting to speculate on the reason for the enuresis. The mass in the bladder wall probably interfered with the neuromuscular mechanism of the bladder sphincter. While it could not be compared with the urgency due to a badly infected bladder with a loose stone, it is reasonable to assume that this mass did have a certain amount of mobility which contributed to the disturbed function. This conclusion is supported by the clinical improvement of the patient following removal of the calculus.

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PULMONARY LESIONS AFTER ROENTGEN AND RADIUM IRRADIATION*

By ROLF BULL ENGELSTAD

From the Norwegian Radium Hospital

OSLO, NORWAY

IN PREVIOUS papers I have reported on experimental investigations proving that roentgen irradiation produces very marked lesions of the lungs in rabbits.† These lesions are degenerative and inflammatory changes of varying degree, followed by regenerative changes. The lung reaction has a characteristic development, in which four stages can be distinguished:

Stage 1. The initial stage, commencing one to two hours after the irradiation and lasting one to two days. Here we find degeneration of the lymph follicles, changes in the bronchial epithelium with abundant mucus secretion, hyperemia, increased transudation and moderate leukocytic infiltration.

Stage 2. The latent stage, with a duration of two or three weeks.

Stage 3. The main reaction, with marked degenerative and inflammatory changes. The inflammation may be more or less acute, after very large doses often fulminant. The acute inflammation has its maximum one to two months after the irradiation. Subsequently the leukocytic infiltration slowly diminishes and we then find large quantities of macrophages and often a great number of giant cells.

Stage 4. A stage with principally regenerative changes, with proliferation of connective tissue and sclerosis, bone production is not uncommon, and there is a slight proliferation of the bronchial epithelium.

With regard to the radiosensitivity of the lungs of the rabbits I have found:

1. After subepidermicidal doses the lung changes, as a rule, are slight and of short duration.
2. After epidermicidal doses the alterations are very pronounced and leave a marked sclerosis, often with bone production.
3. After still larger, dangerous or lethal doses the lung reaction is exceedingly strong and very often has a fatal outcome.

In view of these experiences it is reasonable to assume that after large roentgen and radium doses lesions of the human lungs will also be found, and in fact, not a few of such cases are reported in the literature, especially in that of the years immediately after the introduction of deep roentgen therapy.

In our own material I have so far found 36 cases which have been interpreted as pulmonary lesions due to roentgen or radium irradiation. I must, however, here and now emphasize that it is very difficult to make an absolutely certain diagnosis of these lesions. In order to make the diagnosis as certain as possible a roentgenogram must be taken before the treatment and it is necessary to watch the patient for several months afterwards, with repeated roentgen examinations.

The clinical symptoms are not very characteristic. During the treatment, or a short time afterwards, the patient develops a cough, which can be very annoying, and sometimes also fever. Pains in the chest are not common. The physical examination does not usually reveal any pathological changes, and it is only in a few cases that signs of pulmonary infiltration are found.

The findings at the roentgen examination vary. Most commonly irregular spotted or striped shadows are seen, in some cases also a more diffuse infiltration. The

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

† Engelstad, R. B. Ueber die Wirkungen der Röntgenstrahlen auf die Lungen. *Acta radiol.*, suppl. 19, 1934, pp. 1–94.

Fig. 1. Case 1. Male, aged sixty-six, carcinoma of the esophagus. Before treatment.

shadow stripes may have a fan-shaped arrangement, radiating from the hilum into the lungs. The roentgen picture may, in other cases, be mistaken for pulmonary metastasis. After some weeks these changes begin to diminish little by little, and in a

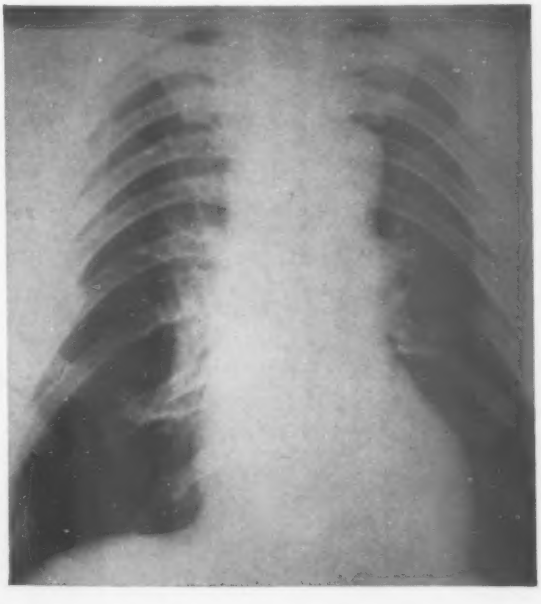

Fig. 2. Case 1. After roentgen treatment over four fields, total dose 8,240 r, daily dose 100–200 r.

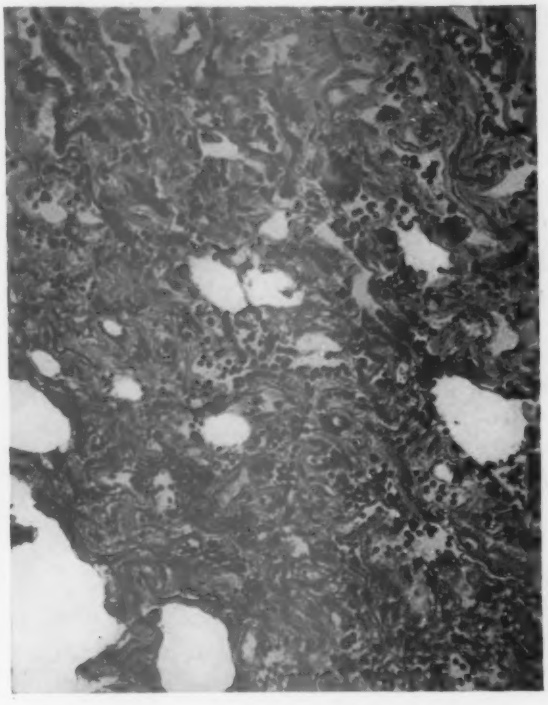

Fig. 3. Case 1. Showing hyperemia, edema, lymphocytic and leukocytic infiltration.

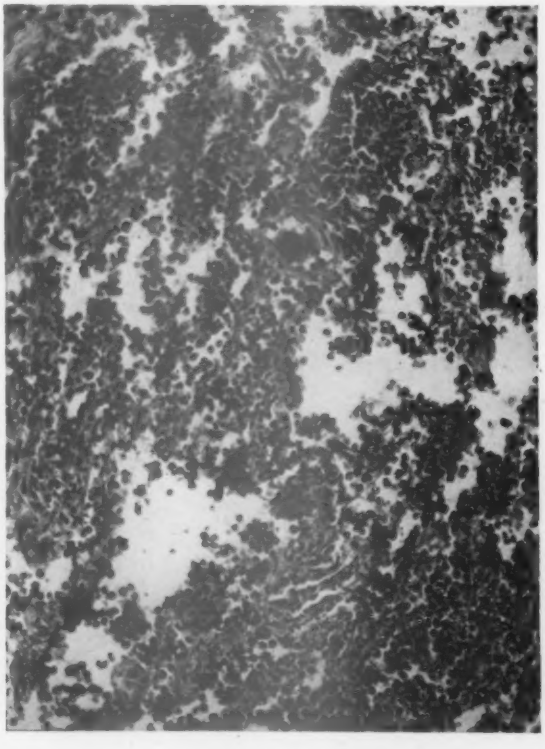

Fig. 4. Case 1. Showing lymphocytic infiltration.

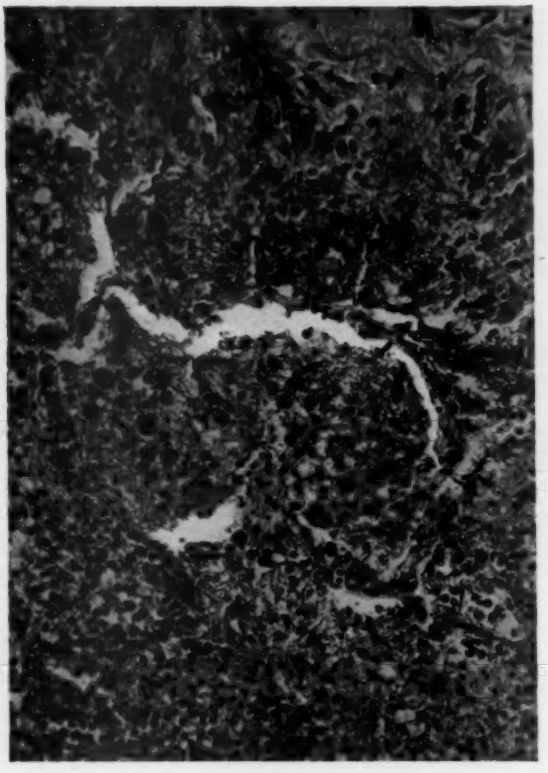

Fig. 5. Case I. Showing lymphocytic infiltration and macrophages.

few cases they disappear completely. As a rule, however, sharply outlined spots and

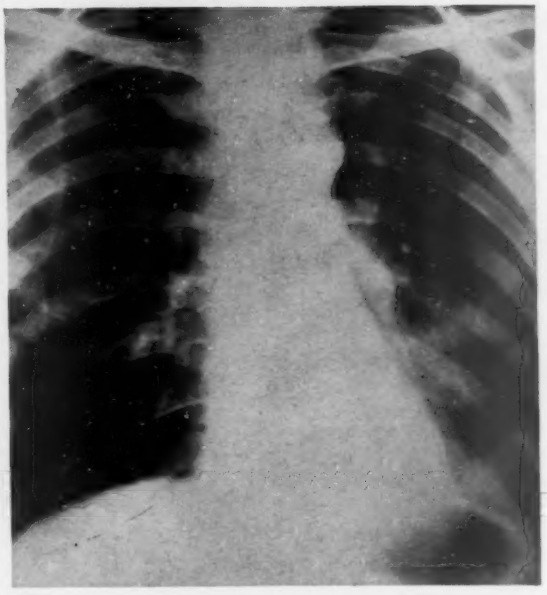

Fig. 7. Case II. After roentgen treatment over two fields, total dose 4,600 r, daily dose 200 r.

stripes are found in the late stages, as a result of the fibrous changes following the reaction. Retraction of the irradiated side may be seen. Thus, the roentgen findings do not differ in any characteristic manner from those in other inflammatory diseases of the lungs. The diagnosis of the radiation lesions of the lungs can therefore only be

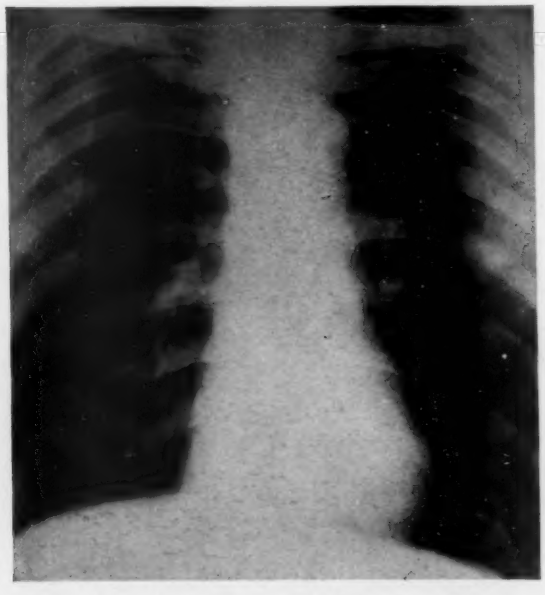

Fig. 6. Case II. Male, aged sixty-seven, carcinoma of the esophagus. Before treatment.

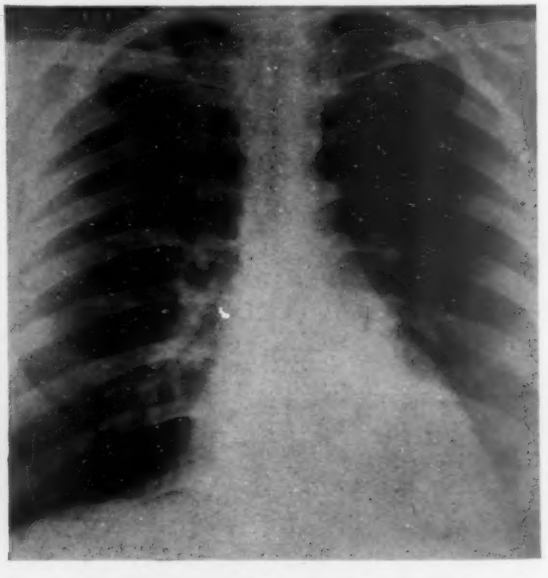

Fig. 8. Case III. Female, aged forty-eight, carcinoma of both breasts. Before treatment.

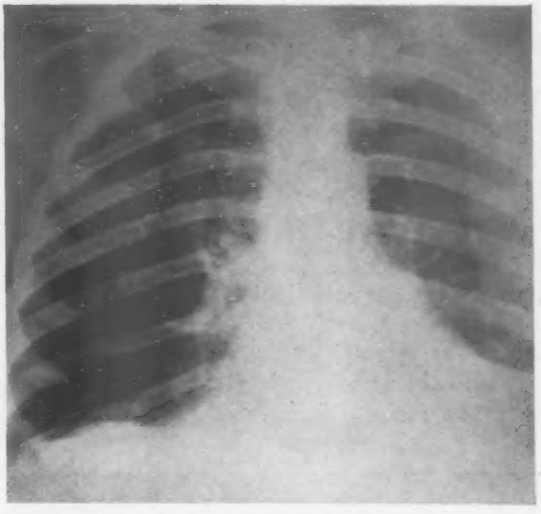

Fig. 9. Case III. After radium treatment (three years, several series). Dose: 36+55+36+6+42+41+37+30+30 Dominici units.

made after protracted observation of the patient.

In most of our cases the clinical and roentgenological symptoms have been moderate, but we have also seen very pronounced reactions. It is impossible here to give a detailed description of all of our cases; I will therefore confine myself to demonstrating some typical examples.

Case I. Male, aged sixty-six, with esophageal carcinoma. Roentgen treatment over four fields,

Fig. 10. Case IV. Female, aged fifty, carcinoma of right breast. Before treatment.

Fig. 11. Case IV. After roentgen treatment, total dose 3,420 r, and radium treatment, total dose 46+30 Dominici units.

total dose 8,240 r, daily dose 100–200 r. Before the treatment no pathological changes in the lungs. After the treatment signs of pulmonary infiltration, partly as a homogeneous slight shadow, partly as a more irregular infiltrative process. The patient died marasmic three months after the treatment. In the irradiated parts of the lungs the microscopical examination revealed foci of a marked fibrosis and of leukocytic and lymphocytic infiltration as well as large quantities of macrophages (Figs. 1–5).

Case II. Male, aged sixty-seven, with esophageal carcinoma. Roentgen treatment over

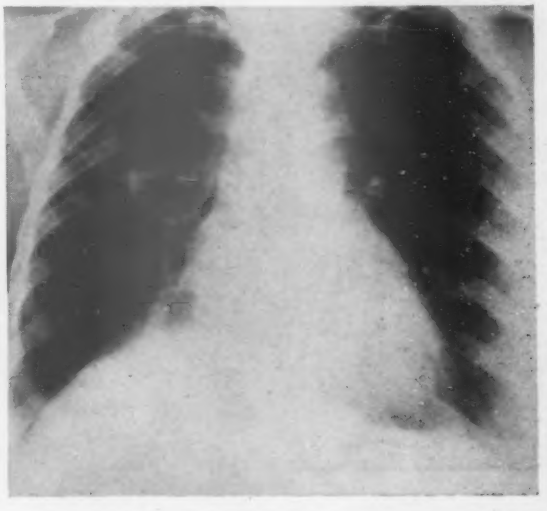

Fig. 12. Case IV. Eight months after treatment.

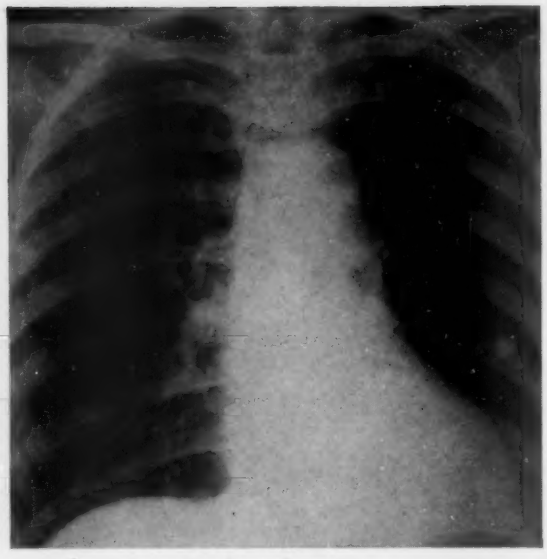

Fig. 13. Case v. Female, aged fifty-eight, recurrence after operation for carcinoma of the right breast. Before treatment.

two fields, total dose 4,600 r, daily dose 200 r. Roentgen examination before the treatment: a calcified focus in the right lung, but no other pathological changes in the lungs. After the treatment a widespread infiltration was found in the lower part of the left lung (Figs. 6 and 7).

Case iii. Female, aged forty-eight, with carcinoma of both breasts. She was given during the course of three years several series of radium treatment with very large total doses (36+55+36+6+42+41+37+30+30 Dominici units). Roentgen examination before the treatment: normal lungs. After the treatment: infiltration in both lungs, especially in the left (Figs. 8 and 9).

Fig. 14. Case v. After teleradium treatment with large doses.

Case iv. Female, aged fifty, with carcinoma of the right breast. Treated with roentgen rays, total dose 3,420 r, and with radium 46+30 Dominici units. Roentgen examination before the treatment: a calcified focus in the right lung, but no other pathological changes. After the treatment: a conglomeration of infiltrations,

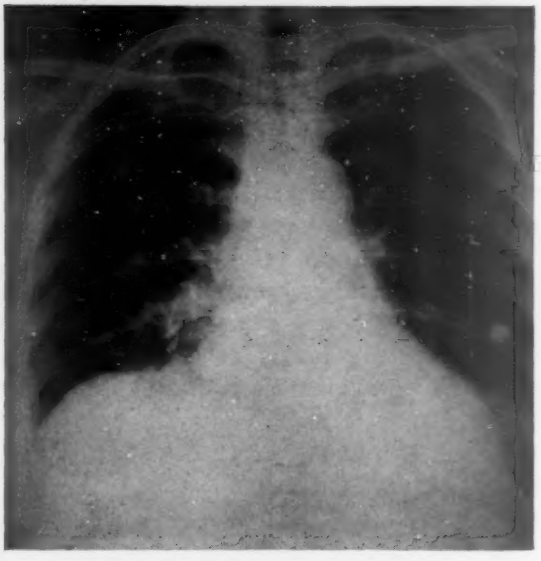

Fig. 15. Case v. Six months after treatment.

increasing in size during the immediately succeeding months and then diminishing, leaving a dense, sharply outlined, star-like infiltration (Figs. 10, 11 and 12).

Case v. Female, aged fifty-eight, with carcinoma of the right breast. She was operated upon, had recurrences and was treated with teleradium at another hospital. Roentgen examination before the treatment: a calcified focus in the left lung, but no other pulmonary infiltration. After the treatment: a widespread infiltrative process in the right lung with a network of shadow stripes. Some months afterwards the infiltration began to diminish and was followed by a pronounced fibrosis with shrinking of the lung (Figs. 13, 14 and 15).

The 36 patients having a demonstrable lung reaction, were treated for the following tumors:

	Cases
Carcinoma of the breast	21
Carcinoma of the esophagus	10
Pulmonary metastasis from extrapulmonary primary tumors	4
Primary carcinoma of the lung	1

During the same period of time 386 cases of breast carcinoma and 49 cases of esophageal carcinoma have been treated. The frequency of the radiation reaction in the lungs is thus:

Carcinoma of the breast	5.4%
Carcinoma of the esophagus	20.4%

All the patients with esophageal carcinoma have had roentgen treatment, mostly over four fields and usually with a total dose of 8,000–10,000 r. Most of them have also been treated with radium in a sound in the esophagus.

In the cases of breast carcinoma the treatment has been:

	Cases
Roentgen treatment	5
Radium treatment	11
Roentgen and radium treatment	5

The radium treatment was in some cases given as a teleradium treatment, the radium-skin distance being 5–6 cm., but in most cases with radium on a mould, the distance being 3 cm. Usually an epidermicidal dose was given. When roentgen treatment was used, it was always given as a tangential irradiation.

The pulmonary tumors were all treated with roentgen rays. The roentgen treatment was in these, as in all the other cases, prolonged and fractionated, with daily doses of 100–200 r and a total dose up to 13,000 r, the number of fields varying from two to six.

The conclusion that can be drawn from this investigation is that in irradiation of the thorax, in mammary carcinoma, esophageal carcinoma, mediastinal and pulmonary tumors, one must count on the possibility of a pulmonary lesion caused by the roentgen or gamma rays, particularly when several fields are irradiated and an epidermicidal dose is given. After small doses pulmonary lesions are not seen. In our material very large doses of roentgen or gamma rays have been used in almost all the cases where a radiation reaction was demonstrated in the lungs.

The radiosensitivity of the human lung seems to correspond rather well with that of the rabbit. The histological findings also seem to be similar to those in rabbits.

The subjective, physical and roentgenological symptoms are not very characteristic and a prolonged period of observation is necessary in order to make the diagnosis. Pulmonary injuries with fatal outcome due to irradiation have in our material not been observed.

RADIATION REACTION IN THE LUNG*

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INTRODUCTION

WHILE it was noted as long as forty years ago by Bergonié and Tessier[1] that intensive irradiation of the thorax could produce an inflammatory reaction in the lung, and scattered clinical and experimental observations have been made since, there has been but little progress in our understanding of this field. In fact, until recently, many radiologists have been inclined to regard with skepticism the existence of pulmonic changes resulting from therapeutic irradiation.

The first series of experiments primarily focused on the effect of radiation on the lungs was carried out by Wohlauer[19] on 10 guinea pigs. They received doses ranging from 7.5 times the dose required to produce dermatitis to a fraction of that dose. He regarded pulmonary hyperemia and recent and old hemorrhages as evidences of radiation effect. In addition, there was slight leukocytic exudation into the alveoli in some of the animals as well as some dilatation of the perivascular and peribronchial lymphatics, which he regarded as probably secondary to the congestion. He interpreted the absence of alteration in the alveolar lining cells as an indication of their refractoriness to roentgen rays.

Early studies were focused on the effect of radiation on pulmonary tuberculosis rather than on the lungs themselves. A series of experiments by Küpferle[11] and others from 1912 on brought out the fact that there was more fibrosis adjacent to the tuberculous process in the irradiated animals than in the controls. The amount of radiation and the time consumed in giving it varied considerably.

In the course of a series of experiments on the effect of radiation on the gastrointestinal tract, Warren and Whipple[16] exposed the thoraxes of 3 dogs to medium wave roentgen rays in amounts from 350 to 450 ma-min. There was no clinical or postmortem evidence of pulmonary damage, although there were marked changes in the gastrointestinal tract.

Hines[9] was the first to recognize radiation reaction of the lungs in his report of autopsy findings in 2 cases of supposed radiation reaction of the lung in 1922. The microscopic lung changes in the first case are of uncertain character, being complicated by widespread pulmonary metastases from a sarcoma of the arm. The patient, a male aged forty-six, received approximately 5,000 ma-min. at 140 kv., 20 inch distance, with a filter of 1 mm. copper and 1 mm. aluminum and 2,400 ma-min. at 125 kv., 12 inch distance, with a filter of 10 mm. aluminum. The right lung, weighing 1,100 grams, showed dense pleural adhesions which were absent from the left. The left, weighing 1,000 grams, was described as dry, tough, and brown. Both lungs contained numerous metastases. Aside from widespread tumor infiltration, microscopic examination showed obliteration of many alveoli by fibrosis of their walls and hyperplasia of the perivascular and peribronchial connective tissue. The author also mentions edema of alveoli and some epithelial desquamation. These changes may occur in many different conditions and in this case the sequence of cause and effect is not clearly demonstrated. It is our opinion that the changes described in his second case may be due to metastatic malignancy rather than to the very small amount of radiation which was given.

Groover, Christie and Merritt[8] reported the clinical and roentgenographic findings in one case of pleuropneumonitis ending

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in clinical evidence of fibrosis following roentgen therapy of the chest for mammary cancer. They mention but do not describe transient changes in other cases. Cough, respiratory embarrassment, and increased roentgenographic density of the lungs developing at about the height of the cutaneous reaction and subsiding in six to eight weeks were noted following treatment with roentgen rays generated at 8.5 to 9.5 inch spark gap, 12 inch focal skin distance, and filtration through 0.5 mm. copper and 1 mm. aluminum in each field.

Wintz[18] pointed out that irradiation of mammary and pulmonary cancer particularly tends to produce pulmonary change. Evans and Leucutia[5] showed that lung changes are dependent on the quantity of radiation rather than on its wave length. One case of clinical radiation pneumonitis and 2 autopsies of irradiated chest cases which showed thickening of alveolar walls were reported by Fike.[6]

Desjardins,[2] in his review of the effect of radiation on the heart and respiratory system, mentioned that he had seen some degree of pleuropneumonitis in "about 2.5 per cent of several hundred patients, in which the thorax was irradiated for 40 or 45 minutes (800 r to 1000 r in air), but has never seen such reaction after exposure for 30 minutes (600 r in air), even when repeated several times at intervals of three or four weeks."

In 1934 a group of 4 cases of pulmonary radiation reaction, only one of which came to autopsy, was reported by McIntosh[12] together with 4 other probable cases. In the one autopsied case, an inoperable carcinoma of the breast was treated with over 10,000 r at 200 kv. The size of the portals was not reported. About ten weeks after the first treatment a cough developed. After three months, additional radiation was given and ten days later the patient developed a fatal bronchopneumonia. The lungs showed thickened pleurae with fibrinopurulent pleuritis. The lung parenchyma showed consolidation with dense, patchy, dull white foci, many in relation to the smaller bronchi. Definite peribronchial fibrosis was present. Microscopic sections showed thickening of the alveolar walls, some exfoliation of the lining cells and perivascular and peribronchial thickening in all sections. The nature of the "thickening" was not specified. Widespread pneumonia was also present.

Transient radiation changes were detected by clinical and roentgenographic means by Downs[3] in 11 out of 53 cases of carcinoma of the breast in which the chest had been irradiated. There were no postmortem observations. Seven of the cases had received more than 7,000 r and 4 cases more than 10,000 r. The changes were transient in all but one case, a female aged sixty-nine, who had had radium needles implanted in the axilla.

Engelstad[4] reported lung changes interpreted as resulting from radiation in 21 (5.4 per cent) of 386 cases of irradiated breast carcinoma and in 10 (20.4 per cent) of 49 cases irradiated for carcinoma of the esophagus. Cases of radiation reaction followed large dosages, some from 6,400–13,000 r. One of the described cases was autopsied.

While clinical and roentgenologic pulmonary changes have been reported following heavy external irradiation in various cases (Hsieh and Kimm[10] among others), supporting pathologic observations are few or absent.

Most of the observed cases have been associated with radiation treatment of carcinoma of the breast. Thirty-six such cases were found by McIntosh and Spitz[13] among 60 followed clinically and roentgenologically. Autopsies were obtained in 6 cases, as well as one additional case due to irradiation of chest metastases in a child five years of age. The pathologic findings, though briefly reported, are in accord with those usually described: "Histologically the alveolar walls were generally thickened; the alveolar epithelium was desquamated into the air vesicles. Definite increase of perivascular and peribronchial connective tissue was present.

The bronchial lymph nodes were hemorrhagic and in places necrotic. Scattered lymphocytes were found throughout." Fifteen of the cases were severe, as judged from the films, and two-thirds of these showed symptoms two to six months after treatment. The milder grades of radiation pneumonitis were symptomless. One fatal case has been reported by Rajewsky[14], a twenty-four year old worker in a radium plant, who was exposed for three years and died after two years of dyspnea and weakness. His lungs showed "diffuse induration, with spots of fibrous hepatization and carnification."

While some radiologists have recognized the roentgenological picture and clinical symptoms of pulmonary changes subsequent to irradiation as forming a fairly distinct entity, little definite evidence has accumulated as to the factors which determine the onset, permanence, and duration of radiation pneumonitis. The rare postmortem observations on these cases are disappointing and reveal only vague changes, chiefly of a chronic nature, which seem to obscure still more rather than to illuminate the process. But all these observations seem to have established beyond doubt the fact that the lung, like other tissues—as skin or mucous membrane—often suffers from residual changes following treatment with radium or roentgen rays which may be prejudicial to the patient's health. Clinical evidence points to two types of changes, one transitory and the other permanent. Since the pathology of these changes has received little attention, it seemed worth while, in view of the ever increasing use of radiation therapy, to attempt to define more exactly their nature and incidence.

PRESENT STUDY

Our method of procedure has been, first, selection, on a histologic basis, from our autopsy series, of the lungs which showed changes which we considered due to irradiation; second, verification of these by history; third, correlation of histologic, gross, clinical, and radiation factors in these cases; and finally, reconstruction of the sequence of histologic changes of radiation pneumonitis.* Complete records of typical cases will be appended.

The pulmonary alterations which first attracted our attention occurred in a case (Case III) in which, although the amount of radiation given was not great, the changes could only be interpreted as due to radiation. This case will be presented in detail later. It must be borne in mind in discussion of the histologic changes following irradiation that unique histologic reactions are almost unknown. It is chiefly through typical combinations of cellular changes or the presence of the causative agent, as amoeba, spirochete, bacillus, etc., that the pathologist recognizes and classifies disease processes. The salient points which we have used in differentiating radiation reaction from other inflammatory changes in lungs are: (1) a hyaline membrane closely adherent to alveolar walls and never present alone but always associated with one or all of the following changes; (2) swollen alveolar lining cells either with or without desquamation and fibrosis, edema, or mild inflammatory exudation in the supporting tissue; (3)edema without appreciable inflammatory reaction; (4) diffuse alveolar fibrosis without evidence of organizing pneumonia, tuberculosis or silicosis; (5) an unusual fibrillar hyalinization of alveolar walls; (6) hyalinization of arterial walls; (7) interalveolar capillary changes such as swelling of endothelium and thrombosis. All of these changes are frequently seen in one section, but there is great variability in their degree and extent. These criteria and their relative values will be discussed later.

We have reviewed all the cases (398) with tumors situated between the diaphragm and the neck coming to autopsy in the Huntington, Deaconess, and Pondville Hospitals. The lung slides on these 398 cases were reviewed and classified on the

*By pneumonitis we mean an inflammatory response involving the parenchyma of the lung and not restricted to the alveoli.

basis of the histologic picture presented, using the above changes as guides, into three groups—positive, suggestive, negative—according to whether the changes present were considered referable to irradiation. Throughout this discussion it is important to keep in mind the nature of our material. The sections were often taken without reference to lobes. In many of the cases there was little lung tissue which was not involved by tumor. Samples taken without reference to the irradiated field may be inadequate for such a study as this.

The autopsy protocols, histories, and roentgenograms of these cases were then studied. In this group, 234 of the cases had received some irradiation over the thorax and 163 had not received any type of irradiation which could possibly affect the lungs. The irradiated cases had received from 15,000 to 800 r; a few of the cases of breast cancer had been treated by implantation of radium needles only. To our surprise only 3 of the 31 cases which we had classified on a purely empirical basis as radiation pneumonitis had not been irradiated. This gave greater confidence in our criteria in view of the fact that there were many cases of aspiration pneumonia and chronic pneumonitis in the group which might be supposed to confuse the picture. The relation of the presence of reaction to the amount of radiation will be discussed later.

While the gross observations as described in the protocols were often unsatisfactory and difficult to evaluate, none the less, certain significant changes were occasionally described. Most important was a dry, rubbery texture, the lungs being noncrepitant or only slightly crepitant, and tending to be pale with a suggestion of diffuse fibrosis. In some of our cases pleural fibrosis was absent, and in none could its existence be ascribed to irradiation alone. Pleural fibrosis is induced by so many agents that a causal relationship to irradiation is difficult to establish with certainty in any given patient. A few of the lungs were slightly edematous and congested, suggesting interstitial pneumonitis.

In most cases adequate, and in many detailed, histories were available. From this standpoint, a nonproductive cough was the most important symptom, although dyspnea and chest pain were also significant indications of pulmonary changes. In this respect our findings coincide with those so adequately described in the literature.

Evidence of lung changes based on a study of roentgenograms of the chest was less satisfactory, since only 62 of the 163 cases had had chest films taken two months or more after therapeutic irradiation. In 53 other cases of this group post-irradiation chest films were taken at such short intervals after irradiation as to be inconclusive. In 36 of the 62 cases the presence of bronchopneumonia, metastatic tumor, or fluid so masked the picture as to render the determination of radiation changes impossible. Five cases (8 per cent) showed evidences of radiation reaction—pleuropulmonitis, progressive fibrosis of the irradiated lung field, or traction of the mediastinum.

The amount of radiation, symptomatology, and pulmonic change are correlated in the tables. In these tables we see that the cases are restricted to a relatively small group, the breast carcinomas naturally predominating because of the greater frequency of thoracic irradiation in this relatively common type of neoplasm. Since roentgen therapy to bronchial and esophageal neoplasms can only be achieved by traversing at least a part of the lung, these cases also frequently show radiation reaction.

In correlating these factors it became apparent that acute, late, and combined acute and late types of reaction could be recognized. The time intervals during treatment and from irradiation to death in large part determined the type of reaction found on postmortem examination, explaining the absence of reaction in some cases which had received large amounts of radiation.

TABLE I

CASES SHOWING PULMONARY RADIATION REACTIONS

A. Acute Reactions

a. Definite

Case No.	Location of Tumor	Age	Sex	Treatments					Interval between First and Last Series of Irradiation	Interval from Last Irradiation to Death
				Date	Amount	Total Amount	Portals	kv.		
I	Breast	58	♀	Oct. 1936 Dec. 1936 Jan. 1937	1,200 r 2,800 r 600 r 1,800 r	6,400 r	Large Small Small	400	12 weeks	16 weeks
II	Breast	52	♀	Apr. 1930 Oct. 1930	3,200 r 1,600 r	4,800 r	Large	180	22 weeks	8 weeks
III	Mediastinum	56	♀	Oct. 1936 Dec. 1936 Feb. 1937	1,200 r 1,200 r 120 r	2,520 r	Large	200	20 weeks	1 day
IV	Breast	86	♀	Sept. 1934	600 r	600 r	Large	200	—	6 days

b. Suggestive

V	Esophagus	79	♂	Jan.–Feb. 1932	3,000 r	3,000 r	Large	200	4 weeks	10 days
VI	Esophagus	53	♂	Dec. 1933	3,600 r	3,600 r	Small	200	4 weeks	2 weeks
VII	Breast	45	♀	May 1934 June 1934	1,200 r 17,320 mg-hr.		Large	180	4 weeks	12 weeks
VIII	Breast	47	♀	Aug.–Sept. 1933	1,800 r	1,800 r	Large	200	3 weeks	52 weeks
IX	Lung	46	♂	Aug.–Sept. 1937	1,200 r	1,200 r	Small	200	3 weeks	4 weeks

B. Acute and Late Radiation Reactions

a. Definite

Case No.	Location of Tumor	Age	Sex	Treatments					Interval between First and Last Series of Irradiation	Interval from Last Irradiation to Death
				Date	Amount	Total Amount	Portals	kv.		
X	Breast	55	♀	May–June 1936 Nov.–Dec. 1936– Jan. 1937	3,800 r 2,600 r	6,400 r	Large	200	32 weeks	3 days
XI	Breast	50	♀	Sept.–Oct. 1936	3,600 r	3,600 r	Large	180	4 weeks	8 weeks

Table I (*Cont.*)

B. Acute and Late Radiation Reactions (*Cont.*)

a. Definite (*Cont.*)

Case No.	Location of Tumor	Age	Sex	Treatments					Interval between First and Last Series of Irradiation	Interval from Last Irradiation to Death
				Date	Amount	Total Amount	Portals	kv.		
XII	Breast	54	♀	Dec. 1930 Jan. 1931 May 1931	1,400 r 2,000 r 1,200 r	4,600 r	Large	200	35 weeks	8 weeks
XIII	Breast	39	♀	Dec. 1931– Nov. 1932	8,000*– 9,000 r		Large	180	52 weeks	1 week
XIV	Esophagus	70	♂	Feb.–Mar. 1937 May 1937	6,400 r 1,800 r	8,200 r	Small	200	11 weeks	4 weeks
XV	Breast	43	♀	July–Oct. 1931 Apr.–July 1932 Dec. 1932 Feb.–Mar. 1933	3,200 r 1,600 r 800 r 800 r	6,400 r	Large	180	84 weeks	12 weeks
XVI	Breast	62	♂	Dec. 1935– May 1936 Aug. 1936 Oct. 1936	7,000 r 3,600 r 2,400 r	13,000 r	Large	200	39 weeks	9 weeks
XVII	Bronchus	61	♂	Mar. 1936 Apr. 1936	1,600 r 900 r	2,500 r	Large	200	2 weeks	5 weeks
XVIII	Breast	41	♀	Nov. 1927 May 1928 July 1932	600 r 600 r 1,000 r	2,200 r	Large	170	230 weeks	2½ years
XIX†	Breast	52	♀	May–July 1937	7,900 r	7,900 r	Large and small	1,000	8 weeks	26 weeks

* This represents approximate amount. Exact amount not known, as much of treatment was received in other hospitals.
† This case was first observed clinically. It is not one of the group of 398 cases studied primarily from the histologic angle.

b. Suggestive

XX	Mediastinum Breast	35	♀	Feb.–Mar. 1931	15,000*– 16,000 r		Large	180	108 weeks	8 weeks
XXI	Bronchus	68	♂	Apr. 1934 June 1934	4,000 r 4,000 r	8,000 r	Small	180	11 weeks	12 weeks
XXII	Breast	55	♀	Apr. 1935 June 1935 Sept. 1935	3,600 r 1,600 r 2,100 r	7,300 r	Large Small Small	180	12 weeks	29 weeks

TABLE I (*Cont.*)

B. Acute and Late Radiation Reactions (*Cont.*)

b. Suggestive (*Cont.*)

Case No.	Location of Tumor	Age	Sex	Treatments					Interval between First and Last Series of Irradiation	Interval from Last Irradiation to Death
				Date	Amount	Total Amount	Portals	kv.		
XXIII†	Breast	59	♀	Mar.–May 1928 Nov.–Dec. 1928	3,000 r 1,200 r	4,200 r	Large and small	200	34 weeks	20 weeks
XXIV	Breast	49	♀	July 1935 Aug. 1935	1,200 r 500 r	1,700 r	Large	180	4 weeks	16 weeks

* This represents approximate amount. Exact amount not known, as much of treatment was received in other hospitals.
† Lead therapy also.

C. Late Radiation Reactions

a. Definite

XXV	Breast	57	♀	May–Sept. 1930 Mar. 1931 Oct. 1931 Jan. 1932 Mar. 1932	4,800 r 1,200 r 1,600 r 600 r 1,800 r	10,000 r	Large	150 180 200 200 200	96 weeks	12 weeks
XXVI	Breast	64	♀	May–Nov. 1934 Mar.–Apr. 1936	3,400 r 2,100 r	5,500 r	N.S.	200	100 weeks	33 weeks

b. Suggestive

XXVII	Breast	66	♀	Nov. 1934 Jan. 1935 Aug. 1935 July 1936 Feb. 1937	300 r 1,500 r 1,200 r 600 r 1,200 r	4,800 r	Large	200	116 weeks	18 weeks
XXVIII	Breast	53	♀	July 1936	23,112 mg-hr. radium	?			—	1 week
XXIX	Breast	64	♀	May 1932 June 1932	1,200 r 600 r	1,800 r	Large	200	3 weeks	52 weeks

It must be remembered that the time intervals implied in the terms "acute" and "late" are different from those in common usage. As in other types of radiation reaction, "acute" changes may occur months after exposure. Acute here is used to indicate the initial reaction to injury: necrosis and inflammatory change, as distinguished from the later proliferative process of repair. In all tissues reactions following irradiation are slower than most inflammatory responses, and such changes as fibroblastic proliferation may be a part of the initial response to irradiation.

The earliest roentgenographic change seen in our cases was an increase in radiolucency of the chest. This, as in Case XIX, may be followed after an interval of a few weeks by an increased density, part of which is apparent as discrete bands, with displacement of the trachea, heart, and mediastinal shadow toward the affected side (Fig. 7). This early radiation reaction is comparable to that seen in other tissues, such as the skin or mucous membrane and can be expected in some cases to show complete regression and in others to show a residual fibrosis of the lung with or without pleural fibrous adhesions, depending upon the degree of injury and subsequent treatment. The acute reaction may be readily differentiated from infectious lesions by the distinct linear bands associated with the traction of the mediastinum. This usually appears about the same time interval after irradiation that one would expect the height of the cutaneous reaction, although the time is somewhat variable. These distinctive changes also serve to differentiate the process from infiltration of metastatic disease.

Case III developed symptoms of respiratory embarrassment four weeks after the second series of roentgen therapy and fourteen weeks after the first. Roentgen examination of the chest revealed rather extensive changes in the lungs limited somewhat to the field irradiated. The small amount of radiation given and the absence of distinctive changes in the film led us to consider infiltration of malignant disease rather than radiation reaction. It must be kept in mind that the later stages of the acute reaction may not be distinctive. Moreover, in view of the known presence of Hodgkin's disease in Case III it was natural to consider this change as due to malignant infiltration and further roentgen therapy was carried out. Study of lung sections of this case two days after the film was taken showed characteristic gross and microscopic changes similar to the other cases of acute radiation reaction.

The late changes representing the residual fibrosis and hyalinization, often with pleural adhesions and decrease in the size of the thoracic cage, are exemplified by Case XVI. In this phase of radiation reaction one sees fibrous bands as well as varying degrees of traction of the mediastinum toward the affected side. Associated with this is a contraction of the thoracic cage on the affected side. This is due in part to decrease in size of the lung and in part to dense pleural adhesions to the contracted lung. In metastatic disease there is no decrease in size of the thoracic cage, and if pleural involvement occurs as a result of tumor metastasis this is practically always associated with pleural effusion. It is of real value that we can demonstrate radiation changes roentgenologically even in the presence of metastasis. While this often cannot be determined with a single roentgenogram, nevertheless, with serial films it is usually possible to differentiate the development and passing of a radiation reaction from the presence of metastatic disease. Roentgenoscopic studies, lateral chest films and Potter-Bucky films are helpful in distinguishing between radiation pneumonitis and metastatic disease. The percentage of metastasis was the same in both irradiated and non-irradiated groups: 62 per cent and 63 per cent respectively.

The amount of radiation necessary to produce histologic reactions varies greatly, although in most instances heavy dosage is required (Table II). This, together with variations in time and rate at which treatment is given, and the size of the portal, suggests that there are factors other than irradiation alone concerned in the development of these lesions. The variability of time in the development of even the acute lesions is striking. Thus, in the cases showing lesions of the acute type the interval from the first treatment to death ranged from 10 days to 100 weeks and between the last treatment and death the time ranged from one day to twenty-two weeks. In the cases showing combined acute and late types of reaction, the time interval ranged from 11 weeks to 455 weeks from

TABLE II

RADIATION CASES

General					Microscopic Analysis									
					Alveolar Fibrosis			Arterial Changes						
Total Radiation	Case No.	Age	Sex	Time between Last Treatment and Death	Exfoliation of Epithelium	Diffuse	Focal	Hyaline	Intimal Fibrosis	Metastasis	Edema	Pleural Fibrosis	Hyaline Membrane	
16,000–15,000 r	XX	35	♀	8 weeks			+	+	+	+	+			Acute and late suggestive
13,000 r	XVI	62	♂	9 weeks	+	+	++	++	+				++	Acute and late definite
9,000– 8,000 r	XIII	39	♀	1 week	+	+		+		++	+		+	Acute and late definite
	XIV	70	♂	4 weeks	++	+	++	++			+			Acute and late definite
	XXI	68	♂	12 weeks		+	++	+	+	+	+	+	+	Acute and late suggestive
8,000– 7,000 r	XIX*	52	♀	26 weeks	+	+	+		+		+	+		Acute and late definite
	XXII	55	♀	29 weeks	+		+	+	+	++				Acute and late suggestive
7,000– 6,000 r	I	58	♀	16 weeks									+	Acute definite
	X	55	♀	3 days	+	+	++	+	+	+	++		+	Acute and late definite
	XV	43	♀	12 weeks			+			+				Acute and late definite
6,000– 5,000 r	XXVI	64	♀	33 weeks			+	+		+				Late definite
5,000– 4,000 r	II	52	♀	8 weeks	+	+	++	+		++	+		+	Acute definite
	XII	54	♀	8 weeks		+		+		+				Acute and late definite
	XXIII†	59	♀	20 weeks	+		+	+		+	++		+	Acute and late definite
	XXVII	66	♀	18 weeks	+		+	+	+				+	Late suggestive
4,000– 3,000 r	V	79	♂	10 days		+		+			+		+	Acute suggestive
	VI	53	♂	2 weeks			+	+			++			Acute suggestive
	XI	50	♀	8 weeks	+++	++	+	++		+			+	Acute and late definite
3,000– 2,000 r	III	55	?	1 day	+++	+	+	++			++		+	Acute definite
	XVII	61	♂	5 weeks	+	+	+	++	++	++	++			Acute and late definite
	XVIII	41	♀	130 weeks	+	+	+	+		+	+		+	Acute and late definite
2,000– 1,000 r	VIII	47	♀	52 weeks										Acute suggestive
	XXIV	49	♀	16 weeks		+	+		+	++			+	Acute and late suggestive
	XXIX	64	♀	52 weeks		+						+++		Late suggestive
	IX	46	♂	5 weeks	+	+		+	+		+	+	+++	Acute suggestive
600 r	IV	86	♀	6 days	+	+					++		+	Acute definite
Radium														
10,000 r x-ray and 13,861 mg-hr. radium	XXV	57	?	12 weeks	++	++	+	++	+	+		++		Late definite
12,000 r x-ray and 17,320 mg-hr. radium	VII	45	♀	12 weeks	+			+		+	+	+	++	Acute suggestive
23,112 mg-hr.	XXVIII	53	♀	1 week	+++		+++	++	+					Late suggestive
No Roentgen Radiation														
		43	♂		+	++					+		+	
		67	♀		+	+++		+	+	+	+		+	
		76	♀		+	+		+			+			

* This case was first observed clinically. It is not one of the group of 398 cases studied primarily from the histologic angle.

† Lead therapy also.

the time of the first treatment to death. The time interval from the last treatment to death varied from three days to twelve weeks. In view of this wide variation, it can be deduced that in the lung as in the skin there is a wide range of time in which radiation reaction may develop. The variation in development of radiation reaction of the lung is comparable to that seen in tissues subjected more directly to radiation as in intracavitary therapy of the cervix. Hence, even though pulmonic changes sometimes appear long after treatment, radiation pneumonitis should be ruled out before assuming that they are due to metastatic disease.

The question naturally arises as to why some cases which have received comparable amounts of radiation fail to show roentgenographic or histologic evidence of radiation reaction. In an effort to learn what the determining factors might be, the cases were considered from the standpoint of age, thickness of chest wall, whether or not amputation of the breast had been performed, and the presence of pneumonia.

TABLE III

THE EFFECT OF PULMONARY ALTERATION ON PULMONARY RADIATION REACTION

	Metastases		Pneumonia	
	Present	Absent	Present	Absent
Radiation reaction cases	18	11	16	13
Cases without radiation reaction	136	72	76	131

The thickness of the chest wall appeared to have no particular significance (Table IV). Thus, of the cases developing radiation reaction, 15 had a thick wall and 14 a thin chest wall. Of the cases with no radiation reaction, 104 had a thick chest wall and 102 a thin chest wall. Amputation of the breast also made comparatively little difference, 18 of those with radiation reaction having both breasts present and 11 having one amputated on the affected side, whereas among the group showing no pulmonic radiation reaction, 121 had both breasts and 86 had had a breast amputation. Extraneous factors appear to be of little aid in predicting whether a pulmonic radiation reaction will develop in a given case.

TABLE IV

THE EFFECT OF THICKNESS OF CHEST WALL ON PULMONARY RADIATION REACTION

	Chest Wall		Breast	
	Thin	Thick	Amputated	Not Amputated
Radiation reaction cases	14	15	11	18
Cases without radiation reaction	102	104	86	121

Pneumonia was present in 16 (55 per cent) of the 29 cases showing histologic radiation reaction. It was present in 76 (37 per cent) of the cases without radiation reaction whose lungs had been irradiated. Thus there is a slight but possibly not significant difference. We cannot now say anything in regard to the possible hazard of radiation pneumonitis and whether or not it plays any part in the development of pneumonia.

The average ages of the females in the irradiated and non-irradiated groups were identical, 53.6 and 54.2 years. In the males there was a somewhat older average age for the cases showing radiation reaction, 62.7 years as against 51.4 years. We are indebted to Dr. Sidney Farber for a case showing marked reaction roentgenologically and histologically following irradiation of pulmonic metastases of neuroblastoma in a child aged five.

In attempting to differentiate the histologic characteristics of this condition, one must consider changes due to metastatic tumor, atelectasis, complete or partial bronchial obstruction, vascular changes, and to various inflammatory conditions. The features of the acute reaction are three-fold: (1) the striking deposition

of fibrin-like material in the alveoli, often tending to form a hyaline membrane, which may be continuous with the fibrous tissue of the alveolar walls; (2) the swelling and destruction of alveolar lining cells, the survivors being distorted to oval or elongated, swollen bizarre cells, frequently very large and multinucleated; (3) the marked edema. These changes differ from those seen in any of the usual pneumonic processes by the absence of inflammatory cell reaction commensurate with the intensity of the cell changes and edema.

This hyaline membrane is the most definite of all the changes and we have used this primarily in sorting out irradiated from non-irradiated lungs. This membrane is usually distinguished from hyaline change of fibrin masses seen especially in aspiration pneumonia. It is more closely adherent to the alveolar wall, less fibrillar, and more homogeneous than fibrin. The alveoli lined by hyaline are usually much distended in contrast to adjacent alveoli. This membrane is not peculiar to radiation pneumonitis. In the pneumonic form of bubonic plague,[15] a fibrinous membrane may occur at the periphery of the alveolus, but is accompanied by masses of bacteria and hemorrhage. In influenza the hyaline membrane is associated with interstitial emphysema,[20] and frequently acellular or hemorrhagic exudation.[17] In a case dying of an influenza pneumonia, not included in our series, the hyaline membrane was marked and indistinguishable from that seen in the most clear-cut radiation pneumonitis. The early stages of chemical pneumonia (mustard gas, etc.) show at first a hyaline membrane with vascular engorgement, rapidly followed by necrosis and small abscesses.[7]

In the late reaction the vascular change is a help in diagnosis. The marked hyaline fibrosis and the vascular alteration produce not only great thickening of the alveolar walls and resultant separation of the alveolar capillaries, but distinct diminution of the lumina of the larger vessels as well. The latter show the hyalinization and fibrosis of their coats so commonly seen in irradiated vessels elsewhere. There is a diffuse fibrosis of the septa, often focally accentuated, and rarely foci of necrosis of collagen. Late reactions vary in intensity, as seen in Case XIX, in which there is only very slight residual fibrosis of alveolar walls and septa. Such changes are frequently seen in old age, and are not pathognomonic of irradiation.

ILLUSTRATIVE CASES

CASE III (H. H. 37-313). This case illustrates acute radiation pneumonitis. White female, aged fifty-five, was admitted to the hospital September 30, 1936, complaining of dry cough of one month's duration. She was of exceptionally slight build, weighing about 85 pounds. The onset of her present illness was six months prior to admission, consisting of abdominal pains and eructations. Three months before admission the patient had noted a swelling in the neck and thereafter began having night sweats and occasional chills. She also noticed that she readily became fatigued, necessitating her going to bed. After two months she developed a dry cough, sore throat, and became dyspneic. There was some pain throughout the chest, especially on deep inspiration. Physical examination was essentially negative except for several cervical nodes 1 to 3 cm. in diameter and some dullness at the right base. The white blood count was 16,150, the red cell count 4,790,000. The urine was normal. Roentgen examination of the gastrointestinal tract was normal. A roentgenogram of the chest revealed increased density at the cardiohepatic angle. A biopsy of a node in the neck was reported as Hodgkin's disease.

Between October 2 and 10 inclusive, the patient received 600 r to the anterior, and 600 r to the posterior chest through a large portal at 50 cm. focal skin distance, and in addition irradiation to the enlarged cervical nodes. The other factors used were 0.5 mm. copper filter, 200 kv. (peak). On December 14, 1936, the patient was again admitted to the hospital complaining of a constant cough and pain in the lower back. Roentgen examination of the chest showed no changes. In view of the symptoms, the patient received an additional 600 r to the anterior, and 600 r to the posterior chest, using a 20×20 cm. portal.

The final admission was on February 9 due to increasing dyspnea and cyanosis of two weeks' duration. A roentgenogram of the chest revealed a diffuse increased density throughout both lungs corresponding somewhat to the field irradiated (Fig. 1). However, in view of the biopsy diagnosis, the changes were interpreted as due to malignant infiltration by Hodgkin's disease, and she was given an additional 120 r. The dyspnea and cyanosis gradually became more intense, her temperature rose to 101° F., and she died on February 10.

The significant autopsy findings were: A very slight and emaciated female.

Pleural cavities: Essentially negative.

Lungs: Right 430 grams. Pleural surface smooth and pale. Major portion of lower lobe, entire middle lobe, and central portion of upper lobe considerably firmer than normal. On section the increased consistency of the lower and middle lobes is due chiefly to edema, the tissue being pale, turgid and watery. No exudate could be expressed. The firmness of the upper lobe is apparently due in part to atelectasis and in part to a diffuse fibrosis, the consistency being rubbery and firm without any increased fluid content. Left lung 420 grams. Shows similar turgidity of lower lobe and a rubbery firmness of upper lobe. The cut surface has a mottled reddish-white appearance, is quite watery but otherwise resembles the right lung. The upper left lobe is very dry, firm and pale.

Fig. 1. Roentgenogram of chest of Case III, six weeks following irradiation. Note increased density of lung fields roughly corresponding to 20×20 cm. portal used for therapeutic irradiation.

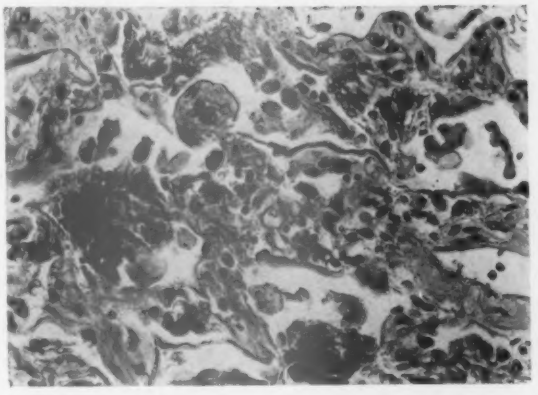

Fig. 2. Photomicrograph of involved portion of lung of Case III, showing changes in alveoli and capillaries. ×600.

Microscopic examination: Sections from different portions of the lungs show marked edema, varying stages of fibrosis and inflammatory reaction, and some necrotic cells. The large bronchi show slight changes consisting of edema of submucosal connective tissue, of bronchiolar walls and of peribronchial connective tissue. The bronchial mucosa is not altered. The alveoli, on the other hand, show marked alterations. The slighter changes consist of some edema of the alveolar walls with swelling, proliferation, and some separation of the endothelial cells and the alveolar lining cells. The alveolar walls range from 2 to 5 times their normal thickness, are relatively acellular, and show edema as well as a fine fibrosis. Changes seen in the capillaries, to be described, are partly responsible for the thickening of the walls. Scattered polymorphonuclear leukocytes, lymphocytes, and macrophages are present in the wall and here and there numerous foam cells lie in the alveoli. Some alveolar lining cells show swelling and proliferation. Others show coagulative necrosis with deposition of fibrin and slight cellular infiltration. Some lie free in the alveolus where they undergo degeneration (Fig. 2). Still others assume bizarre shapes, often multinucleated or vacuolated, with a variable staining reaction.

As a result of the necrosis, wisps or heavy strands of fairly homogeneous material, rarely giving the staining reactions for fibrin, are present. These often sweep rather evenly across the alveolus and sometimes extend from one to an-

other. At times they definitely intermingle with the collagen fibrils of the alveolar walls. At times they fuse with the necrotic remnants of the alveolar lining cells. They are usually crowded to the periphery of alveolar spaces which are dilated, resembling in appearance and location the hyaline membrane seen in influenzal and some other pneumonias (Fig. 3). This material is eosinophilic, shows traces of lipoid, and stains red with Mallory's connective tissue stain. Occasionally slight fibroblastic proliferation occurs

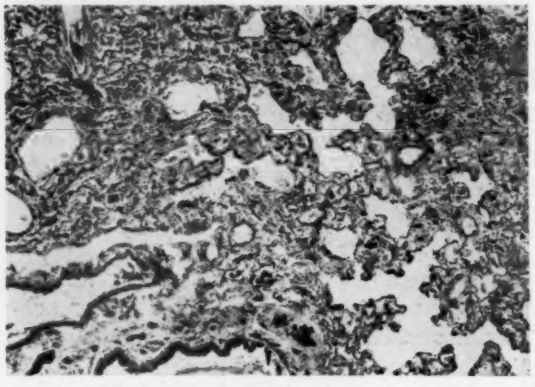

FIG. 3. Photomicrograph of involved portion of lung of Case III, showing hyaline membrane. ×48.

along these strands, sometimes replacing them, simulating but not duplicating the more dense fibrosis seen in the healing of an organized pneumonia. Throughout the lung there are foci of atelectasis, and edema is everywhere prominent. The capillary endothelium is frequently swollen, the lumen diminished, and thus the apparent vascularity of the alveolar walls appreciably lessened. The numerous blood vessels, both arterioles and venules, show edema of the walls, increased fibrosis with a tendency to hyalinization, and increased prominence of endothelial cells. The larger vessels show some edema and hyalinization of collagen, though this is less marked than in the smaller vessels. Agonal thrombi are present in some of the large veins. No evidence of tumor is found.

CASE XXV (N. E. D. H. 16208). This case illustrates a late reaction. White female, aged fifty-seven, was admitted to the hospital June 17, 1931, complaining of a mass in the breast of seventeen months' duration. Biopsy showed carcinoma. The right axillary nodes were involved. From May, 1930, to October, 1931, she received three series of 200 kv. roentgen therapy to the right chest, totalling 5,000 r. During this period she was relieved of pain and gained 8 pounds. The skin of the chest showed some edema and deep tanning in June, 1931. Radium needles were implanted in the right breast and clavicular region June 20, 1931, and 13,861 mg-hr. given. This was followed by further regression of the tumor. In January, 1932, she had some productive cough and dyspnea. She received 1,600 r to the right chest, and in March, 1932, 1,200 r. Roentgenographic examination of the chest at this time showed the left chest fairly clear, the right showing diffusely increased density. The right diaphragm was high and the trachea and mediastinum drawn to the right. Centrally in the right lung was a sharply outlined dense focus. However, the tumor grew rapidly in the skin of the chest, the cough and dyspnea became worse, swelling of the right arm became very marked, and she died on June 26, 1932.

The significant autopsy findings were: A small, poorly nourished elderly female.

Pleural cavities: Right completely obliterated by dense fibrous adhesions, with scattered pockets of serous fluid aggregating 600 cc. Right diaphragm elevated and mediastinum drawn to right. Left pleural cavity shows dense fibrous adhesions in upper portion, 500 cc. of serous fluid in lower. Diaphragm at normal level.

Lungs: Right 240 grams, left 470 grams. Right lung completely atelectatic and adherent to spinal column. Bronchi contain some mucus. On section lung entirely airless, dark red and rubbery. Some dark blood in dependent portions. No gross evidence of metastasis. Left lung partly atelectatic, particularly in upper portion. Parenchyma tough, dark red, but not consolidated. No gross evidence of metastasis.

Microscopic findings: Pleura markedly thickened by fibrous tissue, some dense and hyalinized, some edematous. Many fibroblasts shrunken and distorted. Some blood vessels thick walled and partially hyalinized, others thin walled and dilated. Scattered foci of necrosis, sometimes acellular and showing only a few strands of fibrin, others infiltrated by polymorphonuclear phagocytes and macrophages. Scattered lymphatics contain carcinoma cells in small clusters. Lung parenchyma markedly fibrotic, with scattered persisting alveoli which contain fibrin, foamy alveolar phagocytes, and scattered polymorphonuclear leukocytes. These alveoli are lined by cuboidal or

slightly flattened epithelial cells. The vascularity is diminished, and those vessels present show varying degrees of fibrosis, edema, and hyalinization of their walls. Some vessel walls are five times the usual thickness. There is scattered anthracotic pigment throughout, and scattered clusters of tumor in lymphatics, chiefly perivascular. Bronchial walls are fibrosed.

Case xvi (Pondville 36-A-169). This case shows a severe acute reaction superimposed on a late reaction. The patient, a white male, aged sixty-two, was first admitted December 27, 1935, to the Boston Dispensary, complaining of a growth of the left breast which had gradually increased in size during the past four months.

Local examination revealed a diffuse infiltrating carcinoma involving the left breast extending over the pectoral muscles to the axilla and adjacent chest wall. There were multiple skin nodules involving the left chest wall. In the left axilla there were large metastatic nodes, and also several nodes above the left clavicle

Roentgen examination of the chest showed no evidence of metastases nor of fibrosis.

Between December 27, 1935, and January 6, 1936, the patient received 1,200 r produced at 180 kv. (peak), directed to the left anterior chest, and 1,200 r to the left lateral chest, 300 r daily, using a large portal. Using a 10×10 cm. portal, 900 r was directed to the supraclavicular region. After an interval of two weeks, an additional 1,200 r was given to the left chest and axilla through two portals, and 800 r directed to the supraclavicular region. At irregular intervals, further irradiation was given until June 19, 1936. The total radiation to this date was 7,400 r.

Roentgen examination of the chest revealed a diffuse thickening of the left mid-lung field with pleural adhesions at the base. The changes were thought to be fibrosis as the result of irradiation (Fig. 4). On this date the patient complained of a slight cough. The disease involving the left breast and chest wall showed some regression.

On August 10, 1936, the patient was admitted to the Pondville Hospital and additional radiation was given, a total of 3,600 r, 300 r daily, directed to the anterior, lateral, and posterior left chest.

Roentgenogram of the chest three weeks following completion of this series of treatments showed no change since examination in June. However, a film of the chest taken October 6, 1936, five weeks after last treatment, showed an increase in the changes in the left lung field and some increased density in the right lung root (Fig. 5). These changes were erroneously thought to be pulmonary metastases, and additional radiation totalling 2,400 r was given during the next nine days to the chest, making a grand total of 13,400 r. Following this the patient left the hospital against advice.

Fig. 4. Roentgenogram of chest of Case xvi, after six months of radiation therapy. Note diffuse thickening in left lung field and adhesions at base.

The final admission was on December 3, 1936, at which time the patient complained of continued weakness, and showed signs of progressive inanition until his death on December 24, 1936, nine weeks after the last treatment.

The significant autopsy findings were: A well-developed but extremely emaciated male, showing marked tanning and atrophy of the skin of the thorax, with numerous small tumor nodules.

Pleural cavities: Posterior and lateral aspects of lungs bound to chest wall by dense pleural adhesions. These are tough, fibrous, and are torn loose only with difficulty.

Lungs: Left lung weighs 275 grams. Right lung weighs 300 grams. The outer surface of the right lung is bluish-gray and somewhat mottled in appearance and there are a few

FIG. 5. Roentgenogram of chest of Case XVI, after nine months of radiation therapy. Note increased density of lung fields, especially on left.

tough fibrous tags adherent. The bronchi are diffusely injected. The pulmonary vessels show minimal yellow intimal streakings. On section of the lung, it cuts with increased difficulty. The lower lobe is partially collapsed and is somewhat gray and opaque in appearance. The upper lobe is much more crepitant than the lower lobe and is grayish-red in appearance. The left lung is similar to the right except in section. The lower lobe is firm and on section it is uniform gray with slight yellowish streaks through it. There are adhesions between the upper and lower lobes and the upper lobe itself is crepitant and grayish-pink in appearance.

Microscopic examination: Throughout, fibrosis is extensive, obliterating lung markings in many zones. Edema is definite in almost all regions. Early as well as late organization is present. The walls of the alveoli are markedly thickened and some are represented by eosinophilic hyaline bands.

Many alveoli are diminished in size and some have been entirely obliterated by partially hyalinized fibrous tissue. Many of the smaller persisting alveoli are lined by epithelium sometimes curiously distorted or multinucleated, sometimes cuboidal or elongated. Occasionally foci of lipoid-filled macrophages are seen. There are rare small foci of necrosis with fibrin-like depositions in the denser connective tissue regions. Throughout, the connective tissue is relatively acellular. Blood vessels large and small show marked subintimal thickening and some endothelial proliferation. The capillary lumen is diminished and the alveolar capillaries are separated widely from one another, giving a very definite reduction in the vascular bed.

The arterioles and venules as well as the larger vessels show a marked degree of fibrosis and hyalinization of their walls, not infrequently with regions of mucoid degeneration and a marked diminution in their lumina (Fig. 6). The bronchi and bronchioles show some hyaline fibrosis of the submucosal and peribronchial tissues. The cartilage is unaltered. There is no change noted in the bronchial epithelium or in the mucosal glands. No evidence of tumor noted.

CASE XIX* (N.E.D.H. 37789). This case is of unusual interest from the clinical standpoint. White female, aged fifty-two, was seen at the Huntington Hospital on May 11, 1937. The chief complaint was a lump in the left breast of five months' duration. The past and familial history was unessential. There was no history of cough and no skeletal pains. The local examination revealed in the upper outer quadrant of the left breast an indefinite, deeply situated mass slightly adherent to the skin. The nipple was retracted. There was a large mass of nodes 8 cm. in diameter in the anterior axilla,

* This case was first observed clinically. It is not one of the group of 398 cases studied primarily from the histologic angle.

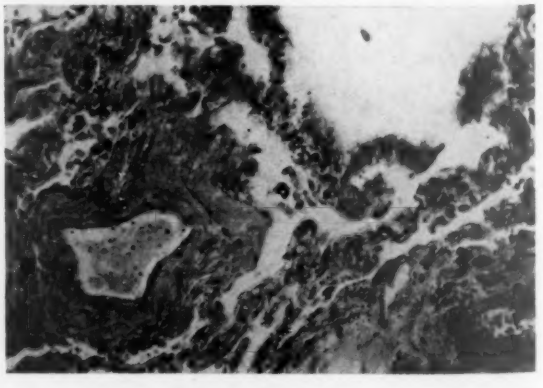

FIG. 6. Photomicrograph of involved portion of lung of Case XVI, showing thickening and hyalinization of vascular walls, atypical alveolar lining cells and thickening of alveolar walls.

and a few 2 to 4 cm. nodes over the left clavicle.

Roentgen studies of the chest, skull, and pelvis were normal. Between May 12 and June 4, the patient received 2,000 r to the left anterior chest and axilla, using a 15×15 cm. portal; 1,600 r to the left supraclavicular area, using a 10×10 cm. portal. The treatments were given in exposures of 400 r daily, using 1,000 kv. (peak) and 70 cm. focal skin distance. At the completion of the treatments no reaction had developed, and there were no new symptoms.

The patient was seen again on June 15. A definite erythema had developed over the left clavicle, and a faint erythema over the left breast and chest. A roentgenogram of the chest showed both lung fields clear with increased radiolucency of the left chest. An additional dose of 2,500 r was given, directed to the left breast and axilla. After an interval of one week, the radiation reaction had increased in intensity, and the masses in the breast, axilla, and supraclavicular region had shown regression. Since the general condition of the patient was satisfactory, 2,400 r additional was given. The roentgen dosage was measured in air with a Victoreen r-meter.

Examination on July 8, the date of the last treatment, showed a desquamation of the skin over the left chest and axilla. There was a slight cough.

Summarizing the irradiation from May 12 to July 8, the patient received a total of 7,900 r directed to the left chest and axilla. In addition, 2,000 r was given to the left supraclavicular area, all in exposures of 400 r each.

The patient was again seen on July 27, at which time she reported a slight cough of about two weeks' duration. Roentgenogram of the chest showed in the peripheral zone of the left upper lung a few ill-defined foci of increased density which were interpreted as changes due to the irradiation.

During the following month, patient continued with a dry cough which gradually improved and the general condition remained unchanged. She was up and about and able to play golf without developing dyspnea. Roentgenogram of the chest on August 31 revealed a diffuse dullness involving the upper half of the left chest. The heart, mediastinum, and trachea were displaced toward this side. Roentgen examination at this time revealed a metastatic focus in the skull and also in the pelvis.

On September 24, the pain in her left hip became so intense she was unable to walk. Roentgen studies of the pelvis revealed a large osteolytic metastasis in the left sacroiliac joint. The changes in the chest demonstrated

Fig. 7. Roentgenogram of chest of Case xix, three months after irradiation was started and one month after last treatment. Note radiation changes in upper left chest, with displacement of heart, mediastinum and trachea to left.

twenty-four days previously had not changed appreciably; however, there was suggestive evidence of diminished density (Fig. 7). Palliative irradiation was given over the pelvis for the relief of pain. The patient was never able to get out of bed after this. The disease in the breast increased in extent. Multiple skin metastases developed over the left chest, extending over the left arm to the elbow. Several nodules developed over the skull and a pathological fracture of a rib occurred. The patient gradually failed, and died on January 9, 1938.

The significant findings at autopsy were as follows: Development and nutrition were good. Weight 130 pounds.

Pleural cavities: Right has a few fibrous adhesions binding lower portion of lung to diaphragm. Rest of surfaces on this side smooth, glistening, slightly injected. Left contains approximately 10 cc. of turbid, straw-colored fluid. Surfaces injected, smooth, glistening except laterally over left lower lobe. Here a thick layer of fibrin binds lung to chest wall.

Lungs: Right 320 grams, left 420 grams. Upper lobes of both lungs slightly subcrepitant. Cut surface gray, mottled with black. Small amount of frothy fluid exudes from cut surfaces. Bronchi patent throughout and contain small amount of thin, frothy fluid. Both lower lobes deep red, definitely subcrepitant, exude much bloody, frothy fluid on slight pressure and show foci of consolidation about smaller bronchi.

Bronchi in these lobes filled with thick, turbid material. Bronchial mucosa is red and finely granular. In the left lower lobe is an ill-defined, soft, gray focus 1.5 cm. in diameter.

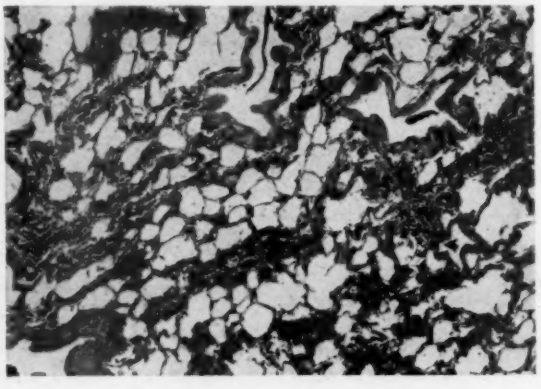

Fig. 8. Photomicrograph of involved portion of lung of Case xix. Note slight fibrosis and hyalinization. ×48.

Microscopic examination: Left upper lobe shows slightly and uniformly thickened and fibrosed pleura. Alveoli empty. The alveolar lining cells are inconspicuous, the alveolar walls slightly fibrotic, the hyalinized connective tissue somewhat dense. This results in an apparent slight lessening of the vascularity of the lung parenchyma. Bronchi contain finely granular material and cellular debris. Epithelial surfaces negative. Bronchial walls slightly fibrosed. Endothelium of blood vessels inconspicuous. Media somewhat edematous in both arteries and veins. A few veins contain mural thrombi. Smaller arterioles present hyaline thickening of their walls. Most of larger vessels show definite fibrous thickening of their walls, usually with some degree of hyalinization (Fig. 8). Left lower lobe shows a similar condition except that the alveoli are filled with finely granular material, polymorphonuclear leukocytes, and a scattering of lymphocytes and mononuclear phagocytes. Some alveoli partly lined by large, pale-staining, oval cells and a few alveoli contain fibrin and cellular debris. Among the exudative cells are scattered vacuolated macrophages. Some of the more heavily affected alveoli contain coarse strands of fibrinoid substance which extend into the connective tissue of the alveolar walls. In scattered foci alveolar lining cells have disappeared or have rarely been replaced by large irregular elongated cells. Bronchi contain similar exudate and show some necrosis of lining epithelium. Right upper lobe shows irregular septal fibrosis and most of alveoli contain a small amount of finely granular material, though a few bordering on bronchi are filled with polymorphonuclear leukocytes, a few lymphocytes and some cellular debris. Bronchi contain similar material and show slight fibrosis of walls. Foci of parenchymal fibrosis with inclusions of large, oval, deeply stained cells are also present. Blood vessels are negative. Right lower lobe somewhat similar to left lower lobe except that inflammatory reaction is more marked and more alveoli are lined by epithelial cells and there is less fibrosis of alveolar walls. No evidence of tumor is found.

Three of the 4 preceding cases we have selected to illustrate the three types of reaction encountered: the acute, the late, and the late with superimposed acute changes. Case xix illustrates the slight, nonspecific changes that may be present after very heavy irradiation and is our only case which has definitely shown a transient reaction as proved at autopsy. From the postmortem studies it would appear either that transient changes resulting from irradiation are not distinguished from other inflammatory conditions or that our material did not include such cases. Considering the wide range of material used in the study, the former seems most likely.

Discussion

This study of radiation pneumonitis from clinical, roentgenologic, and postmortem aspects in an unselected series of 234 patients has served to clarify observations made by roentgenologists as well as to present the sequence of histologic changes underlying the reaction.

The roentgenologic findings in radiation pneumonitis are best interpreted after correlating the clinical course following irradiation with frequent roentgenograms of the chest. It is desirable to have roentgenograms of the chest before irradiation is started, and frequent examinations during the course of the reaction. Under these conditions pulmonary changes due to irradiation can usually be readily differentiated from infections and metastatic processes of the lungs. The practical importance of this type of change is illustrated by Case III of McIntosh[12] and our Case III where the additional radiation given under the assumption that the lung changes were due to metastases may well have been a contributing factor in the death.

The frequency of pulmonic change increases as does the amount of radiation delivered to the chest, but not with any regularity. The majority of the cases showing radiation reaction present symptoms of an unproductive hacking cough during the height of the local skin reactions.

The histologic aspects of the study have been further checked by examination of a control series of 1,060 unselected autopsies from Pondville Hospital from 1929 to 1937 (excluding those used in our initial series of 398 cases taken in part from Pondville Hospital). This control group was handled in the same way as the study group. The histologic diagnosis of radiation pneumonitis was confirmed in 4 cases by the history. There were 3 cases with histologic changes typical of radiation pneumonitis which had not been irradiated. In 5 cases in which there were some suggestive features there had been no irradiation. This percentage of error (0.7 per cent) is as low as can be achieved in differentiating the cause of any histologic reaction not accompanied by the presence of a visible agent. An analysis of our errors shows that these have been due in most cases to acceptance of marked change of one type or another as indicative of radiation pneumonitis. This is particularly apt to be misleading when there is much fibrinous exudate, as in some of the organizing pneumonias.

The sequence of tissue changes following roentgen irradiation of the lungs varies with the amount and kind of radiation. It is probable that the earliest effect is one of mild injury to the alveolar lining cells and the capillary endothelium. Edema, swelling, necrosis, and proliferation of endothelium and alveolar epithelium follow. With injury to connective tissue, fibroblastic proliferation, chiefly in the alveolar walls, occurs. We have not been able to identify peribronchial, septal or pleural fibrosis specifically with radiation pneumonitis.

Our experience shows that appreciable injury and repair of fibrous tissue occur only after very intensive irradiation, the connective tissue apparently being more resistant to roentgen rays than the other tissue elements. The transient radiation pneumonitis long recognized by roentgenologists, and illustrated by our Case XIX, supports this view.

These histologic features of the early reaction, including early fibroblastic proliferation, we have not found distinctive in our cases. With our present knowledge it is not possible to distinguish early acute radiation pneumonitis from other conditions, although very prominent edema and large epithelial and endothelial cells in the absence of much exudate are suggestive of radiation pneumonitis.

When the primary injury is sufficiently severe to affect endothelium, fibrous tissue, and epithelium, the well developed repair process presents a picture which may resemble that following a number of different injurious agents. The vascular change is particularly difficult to evaluate. Fibrous thickening and hyaline swelling of veins and arteries such as are associated with radiation pneumonitis are seen occasionally in youth and more commonly with advancing age, frequently unaccompanied by other disease processes. However, these changes may be restricted to that portion of the lung which presents other evidence

of radiation pneumonitis and which was known to have been included in a field of irradiation.

The only histologic picture which we can with certainty recognize as radiation pneumonitis is that which shows in some degree both these early and late stages in the same lung.

The hyaline membrane which we have emphasized in our classification complicates the subject somewhat inasmuch as we are not at present prepared to describe its manner of formation. It probably represents an acute or subacute response. We feel that this hyaline membrane is the surest guide in diagnosis of radiation pneumonitis. We have rarely been misled by this membrane except when it was slight or atypical and accompanied by organizing pneumonia. Observation of this with the other changes enumerated makes it possible to recognize with accuracy the cases which have received irradiation to the chest. In a few cases we have been led to suspect post-irradiation changes without the presence of the hyaline membrane, only to find that irradiation had not been given. We have found that the other changes we have enumerated as part of radiation pneumonitis are less distinctive and not as easily differentiated from infectious processes.

It is obvious that in going over such a large series of slides accurate grading of relative changes of different types, as fibrosis, edema, endothelial swelling, blood vessel changes, would be an extremely laborious and impractical task. But such a study carried out by a single observer of both gross and microscopic specimens would be of definite value. And it is only by this method of study that we may hope to learn something of the history of cell changes initiated by irradiation.

The fact that a great many heavily irradiated patients show no recognizable reaction makes us feel certain that we still have a good deal to learn of the way in which the lung reacts to irradiation, and the possible hazard of such a reaction. Its relation to pneumonic infections is a particularly important and intriguing question which we are at present unable to answer. We would make this report a plea for more discriminating study of this subject by both radiologists and pathologists. We hope that experiments now being carried on will further clarify the subject.

SUMMARY AND CONCLUSIONS

1. By histologic study of the lungs of an unselected series of 398 autopsied cases of malignant disease primary between diaphragm and neck it has been possible to collect 29 cases (7 per cent of the entire group, 12 per cent of 234 irradiated cases) which showed changes referable to irradiation of the lung. An erroneous diagnosis of radiation reaction was made in 3 cases which it was found later had not received irradiation to the chest. In a consecutive series of 1,060 autopsies (1929–1937) from Pondville Hospital, exclusive of the cases in the first group, there was a 99.3 per cent accuracy in diagnosis of radiation pneumonitis based solely on histologic changes.

2. From the standpoint of its reaction to irradiation the lung should be considered as a highly vascularized mucous membrane of relatively low density.

3. A certain combination of tissue changes presents a histologic picture which is practically pathognomonic for radiation pneumonitis, although the units of cellular and humoral change which make up this picture may be found in other conditions.

4. Tissue reactions most closely simulating radiation pneumonitis are found in: chronic nonspecific interstitial pneumonitis; influenzal pneumonia; chemical pneumonitis; all of which are extremely rare.

5. It is probable that certain stages of radiation response in the lung have not been recognized histologically, and may be of such a nature that differentiation from other disease processes is impossible.

6. The changes may be divided either on pathologic or roentgenographic grounds into three stages: acute, late, and late with superimposed acute reaction.

7. Chest roentgenograms were available in 115 of the 234 cases, but in only 62 cases were they suitable for this study. In only 5 (8 per cent) were there roentgenographic changes definitely due to irradiation. It seems fair to assume that this is not a true index of the frequency of pulmonic reaction. Were radiation changes watched for from the time of beginning therapy, study both antemortem and at autopsy would give a higher percentage of cases showing reaction.

8. Radiation reaction is sometimes slight and may not permanently affect the lung.

9. The amount of radiation alone does not determine the development of a radiation reaction, although the proportion of lungs showing changes increases with the amount of radiation.

10. Variables such as the thickness of the chest wall, amputation of the breast, the existence of pulmonary metastases, the existence of pneumonia, were considered and found to have no significant relation to the development of radiation changes.

11. Age is not a factor. In females no significant correlation with age occurs. In males there was a somewhat higher average age for the cases showing radiation reaction, sixty-five years as against fifty-one years, probably a chance variation.

12. Criteria are given for the differential diagnosis of radiation reaction by roentgenographic and pathologic means.

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PRIMARY LYMPHOSARCOMA OF THE HARD PALATE

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PRIMARY lymphosarcoma of the hard palate is extremely rare. In a review of the literature since 1893, when Kundrat[17] established lymphosarcoma as a disease entity, only one case was found which was limited to the hard palate. Although numerous instances of lymphosarcoma of the hard palate have been published,[4,11,17,20,22] all of these were secondarily involved by contiguity from lesions of neighboring structures. Chaton's case[6] is the only exception. During the past ten years, 108 patients with lymphosarcoma have been registered at the Mount Sinai Hospital. The case reported below was the only one with primary involvement of the hard palate.

CASE REPORT

P. F. (O.P.D. No. 38–69), white, male, aged fifty-four, was admitted to the Out Patient Department of the Mount Sinai Hospital on January 4, 1938.

FIG. 1. Photograph taken on March 22, 1938.

Present Illness. The patient noted a tender, raised "sore" on the hard palate three months before admission which was slowly progressing in size. He had worn a full upper denture for five years, but because of breakage, none was worn for eight months prior to admission. The patient reported infrequent headaches, pain over the malar bones, nasal obstruction and constant post-nasal drip. Generally, his appetite was good, he maintained his weight and slept well. There was no familial history of cancer.

Physical Examination. The patient was well-developed and nourished. He was cooperative. There were two granulomatous circumscribed nodules situated in the anterior half of the hard palate. Both were superficially ulcerated. The larger nodule measured 1 cm. in diameter and was to the right of the midline. The smaller nodule measured 0.5 cm. in diameter. It was situated more anteriorly and to the left of the midline (Fig. 1).

In addition, the patient had bilateral sinus disease and multiple nasal polypi; these polypi were also present in the nasopharynx. There was no regional adenopathy. The chest and abdomen showed no gross evidence of disease.

Laboratory Findings. Hemoglobin 83 per cent (Sahli); red blood cells 4,250,000; white blood cells 8,950, with a differential count of 62 per cent segmented and 4 per cent non-segmented polymorphonuclear cells, 29 per cent lymphocytes, 4 per cent monocytes and 1 per cent eosinophiles. Blood Wassermann reaction was negative.

Roentgen examination of the hard palate with an occlusal film showed no abnormalities. Roentgen examination of the paranasal sinuses revealed marked clouding of all of the sinuses. Roentgenograms of the chest showed no abnormality in the heart, lungs or mediastinum.

The report of the first biopsy of the lesion on the hard palate was as follows: "(61641) Fragment of mucous membrane showing chronic inflammation and epithelial hyperplasia" (Drs. P. Klemperer and S. Otani).

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Course. A provisional diagnosis of nonspecific granuloma was made. Therapy consisted of mouth washes with sodium perborate, liquor alkalinis antisepticus and topical applications of 10 per cent silver nitrate. At first, there seemed to be slight improvement. However, the subsequent course over a period of six weeks showed gradual progression in size.

Biopsy was repeated March 18, 1938: "(62182) Specimen consists of a small fragment of mucous membrane from the mouth. The surface is covered by a slightly thickened squamous cell epithelium having a hornifying layer on its free surface. The submucosa is diffusely infiltrated by cells which are mostly round and more or less uniform. The predominant cell type corresponds to the medium-sized lymphocyte. There are, however, occasional atypical cells and an occasional mitotic figure. Diagnocis: Lymphosarcoma" (Drs. P. Klemperer and S. Otani) (Fig. 2).

Radiotherapy was begun on March 22, 1938. There were 1,800 r (measured in air) delivered to the lesion with the following factors: 200 kv. (peak), 25 ma., 40 cm. distance, Thoraeus filter (0.4 mm. Sn, 0.5 mm. Cu, 4.0 mm. Al), with a half-value layer of 1.8 mm. Cu. These factors produced 22 r per minute. There were 200 r delivered daily through an intraoral cone with a field size of 4.5 by 3 cm.

A week following the last treatment, bilateral nasal polypectomy was performed. Sections of removed tissue were reported "mucous polypi" (62407). Three additional daily treatments of 200 r each were then administered. Total dose to the lesion on the palate was 2,400 r (measured in air). The tumor had practically disappeared twenty days following onset of therapy. At this point, the 600 r additional, mentioned above, were delivered. The reaction was most marked on the sixteenth day and was represented by a mild erythema. The reaction faded gradually and disappeared on the thirty-fourth day, or eleven days following the last treatment. Figure 3 illustrates the reponse to irradiation.

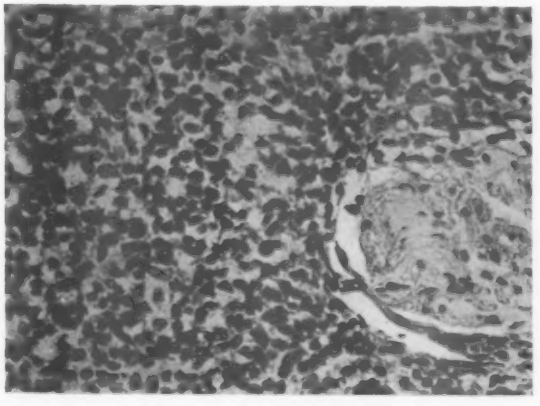

Fig. 2. Photomicrograph of submucosa in the deepest portion of the biopsy section. At the extreme right there is noted a cut nerve around which the diffusely infiltrating lymphosarcoma cells can be seen.

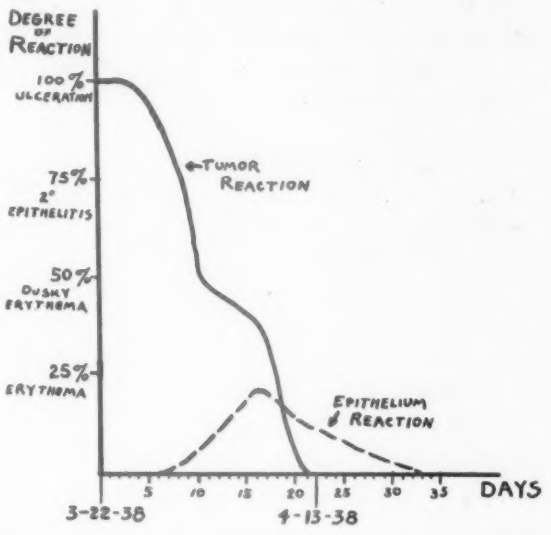

Fig. 3. Response to radiotherapy. The continuous line indicates the tumor size. The interrupted line represents the degree of tissue reaction.

In December, 1938, the patient again reported nasal obstruction and post-nasal drip. Examination revealed recurrent nasal polypi. A partial shrinkage of the polypi with marked subjective improvement resulted from radiotherapy directed over the nose and maxillae. The following factors were used: 140 kv. (peak), 20 ma., 0.25 mm. Cu filter, 30 cm. distance with a half-value layer of 0.48 mm. Cu. A total of 800 r per field at 91 r per minute was delivered through portals 5.0 cm. in diameter.

On May 29, 1939, the patient presented a normal mucous membrane (Fig. 4) over the hard palate with pinhead-sized depressions marking the sites of the original ulcerations. There was no significant peripheral adenopathy. Examination of the chest and abdomen showed no gross evidence of disease. Small nasal polypi were present in the left nasal

FIG. 4. Photograph taken on May 29, 1939.

cavity. The patient's general condition was good.

DISCUSSION

Differential Diagnosis. Many conditions must be considered in a differential diagnosis of a lesion of the hard palate. Of primary consideration are the inflammatory diseases and the neoplasms. The latter may be epidermal, connective tissue, osseous or dental in origin. Of less frequency, metabolic diseases such as osteitis fibrosa cystica, and osteitis deformans of the leontiasis ossea type may occur. Occasionally, developmental malformations such as a nasopalatine cyst[18] are encountered. Misplaced tissue rests such as aberrant thyroid and dermoid cysts[5] may also occur.

In making the correct diagnosis of a lesion of the hard palate, a careful history and physical examination must be supplemented by hematological, serological, bacteriological and roentgen studies, including occlusal films of the palate. Finally, biopsy will usually be necessary to arrive at the exact type of disease present. This may have to be repeated several times if representative tissue is not obtained at first. This is especially true of neoplasms.

Treatment. Surgical excision, electrocoagulation, roentgen and radium therapy have all been used singly or in combination in the treatment of new growths of the palate. Radiation therapy is usually the method of choice in lymphosarcoma. The maintenance of proper oral hygiene is a requisite in the radiation treatment of any mouth lesion. This includes extraction of diseased teeth. There should be limitation of therapy to the lesion either by intraoral cones or by the use of protective devices.[1]

In this case, only roentgen therapy was used. In the case of hard palate lymphosarcoma reported by Chaton, radium element needle implantation was used. He reported complete resolution of existing regional lymphadenopathy without direct treatment of the nodes and marked involution of the local neoplasm. The lymphadenopathy may have been inflammatory. Examination of his patient five months later showed no evidence of malignant disease.

Prognosis. In general, the prognosis of neoplasms of the hard palate is surprisingly good. Bloodgood[3] states, "Lesions of the hard palate are practically identical with those of the gums but are less frequent. Even in cases of long standing and of considerable extent, they rarely metastasize to the lymph glands."

In the case that is being reported, the tumor was slow-growing. For six months prior to treatment, it remained localized to a relatively small area on the hard palate with no extension to regional lymph nodes. The neoplasm was radiosensitive. It disappeared two weeks after the onset of treatment. The patient has been examined routinely every two months since the end of treatment and there has been no recurrence to date, eighteen months after admission.

COMMENT

In analyzing the rarity of primary lymphosarcoma of the hard palate, the

following explanation is suggested. By definition, lymphosarcoma is a malignant neoplasm arising from lymphoid tissue. Whereas the structures of the oral and pharyngeal cavities such as the posterior nasopharyngeal wall, the fauces, the adenoids, the tonsils, and the soft palate are relatively rich in lymphoid tissue, the hard palate is singularly free of this tissue. Quoting Gray's Anatomy:[11] "The palate is covered by a dense structure formed by the periosteum and the mucous membrane of the mouth, which are intimately adherent . . . . On either side and in front of the raphe, the mucous membrane is thick, pale in color and corrugated; behind it is thin, smooth and of deeper color; it is covered with stratified squamous epithelium and furnished with numerous palatal glands, which lie between the mucous membrane and the surface of the bone." Schumacher,[21] in a detailed histological description of the hard palate, also makes no mention of the presence of lymphoid tissue. Therefore, the paucity of lymphoid tissue in the hard palate explains the rarity of its occurrence at this site.

SUMMARY

1. Primary lymphosarcoma of the hard palate is extremely rare and this is probably due to the fact that, normally, the overlying soft parts are relatively free of lymphoid tissue.

2. A case of primary lymphosarcoma of the hard palate is reported which responded favorably to the use of roentgen therapy.

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CARCINOMA OF THE ANUS*

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THOUGH carcinoma of the large bowel has been looked upon as a surgical problem, those malignant lesions found in the region of the anus may be looked upon as an exception. The reasons for such an opinion are based upon anatomical and histological grounds. Therefore, I wish to discuss the problem from the standpoint of the radiotherapist, emphasizing not only permanency of recovery but also the possibility of retention of physiologic function of the anal sphincter.

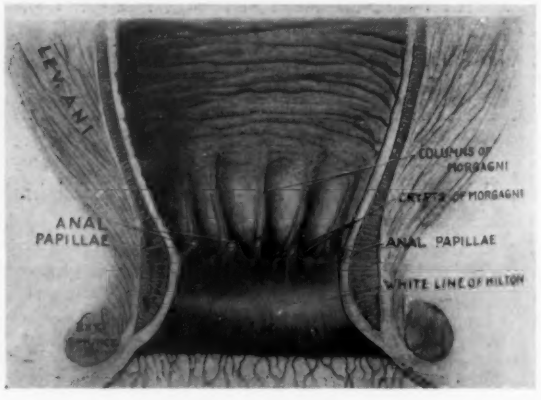

FIG. 1. (From Gant.)

ANATOMICAL CONSIDERATIONS

That part of the terminal bowel which presents itself externally is known as the fixed rectum or anus. Externally it is covered with a loose, coarse, dark-brown pigmented skin, which blends gradually with the skin of the buttocks. Where the junction of the anal skin and the lining mucous membrane takes place (Fig. 1) there is a region known as Hilton's white line; here the skin is soft, smooth, and white instead of pigmented, and covers the region lying between the external and internal anal sphincters. Within the internal sphincter the skin has been replaced by mucous membrane which is redundant and thrown into longitudinal folds, called the columns of Morgagni, the terminal portions of which make up the anal papillae. Here it is that trauma is greatest and infection, inflammation and fissures occur as a result of chronic irritations of various sorts. The surface cells are of the stratified squamous variety, while farther up they are first transitional and then columnar, and the mucous membrane, instead of being in longitudinal folds, arranges itself in transverse folds. Mucus-secreting glands are numerous in the area covered with columnar epithelium, but not very prevalent in the regions where transitional and squamous cells are found. By reason of these histologic facts, malignant tumors found in this section are practically always epitheliomas, though one may see an occasional adenocarcinoma arising above the columns of Morgagni, while the more rare melano-epithelioma may appear on the skin at Hilton's white line.

A matter of great importance is the lymphatic drainage of these structures. In Figure 2 it can be seen that the collecting vessels from the squamous cell covered mucous membrane run toward the anal skin, anastomosing with the subcutaneous lymph vessels around the buttocks and perineum, emptying into the inguinal nodes. Where columnar epithelium is found, the lymph vessels course upward parallel to the hemorrhoidal veins and arteries emptying into the para-aortic nodes, but at that portion where the bowel wall is covered with transitional cells, a "neutral zone" exists, from which lymph may flow in either direction. When an epithelioma attacks the lower bowel the usual direction for metastasis to pass is into the inguinal nodes; however, if the growth is extensive it may, by direct extension, push into the neutral

* From the Los Angeles Tumor Institute. Read at the Twenty-fourth Annual Meeting, American Radium Society, St. Louis, Mo., May 15–16, 1939.

zone (Fig. 2) and thus its cells gain entrance into the para-aortic nodes. Likewise, an adenocarcinoma of the rectum proper may grow down into this same neutral zone, giving rise to metastases that are filtered out in the inguinal nodes. These are important when prognosis is under discussion.

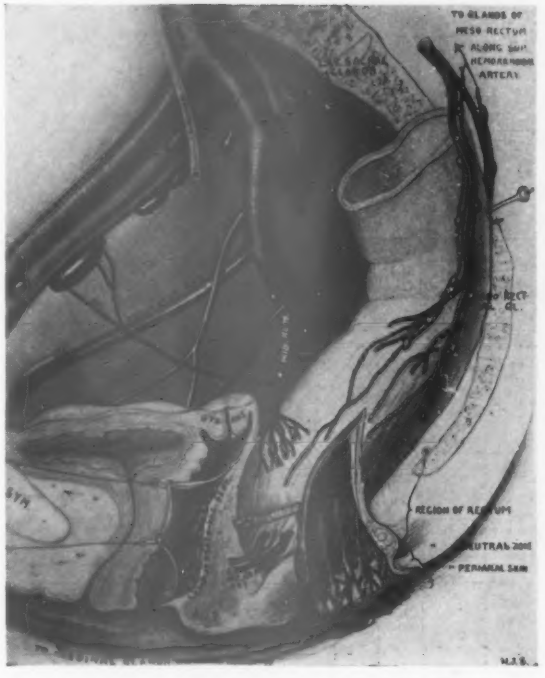

Fig. 2. (From Gant.)

CLINICAL CONSIDERATIONS

In the past fifteen years we have had occasion to examine and treat 260 patients with carcinoma of the terminal colon; of these, 17 had involvement of the anus, giving an incidence of 6 per cent. In these 17 cases we have adequate records for 13 patients; the remainder were terminal cases, so advanced that no treatment, except sedatives, were given; they died very soon after being seen. Though adenocarcinomas may occur here, in these 13 patients, 11 had squamous cell epitheliomas, 1 had a melano-epithelioma and 1 was not biopsied. When grading was done, the majority fell into Grades 3 and 4. The sexes were about equally represented, and only one patient was less than fifty years old—the average age was sixty-four years (Table 1).

The complaint most prevalent was rectal bleeding. This symptom was present for from four to twelve months before medical aid was sought; usually the patient had treated himself for hemorrhoids by the insertion of suppositories and by the application of ointments. One patient had pruritus ani for two years before he developed a non-healing ulcer; another had a rectal prolapse for thirteen years before he developed a growth, while a third had rectal distress for forty years, and multiple fistulae for ten years before a tumor was discovered. The common site for the

Table I

Case and Year	Name	Sex	Age	Symptoms	Description	Pathology	Treatment	Living	Remarks
I 1922	W	F	77	Bleeding 4 mo.	Ulcer 1 cm. anal margin	Squamous cell epithelioma, not graded	High voltage roentgen therapy anus, 300 r; radium—contact, 1 mm. brass filter, 850 mg-hr.	Yes 7 yr.	Not followed any longer
II 1931	R	F	70	Bleeding 8 mo.	Firm tumor completely surrounding anus. Node left groin. Edema left leg	No section taken	Not treated	No	Died in 6 mo.
III 1932	C	M	59	Rectal discomfort 1 yr.	Black, shiny tumor at anal margin 2×3 cm. Small implants in surrounding skin	Melano-epithelioma	Refused treatment	No	Died in 6 mo.

TABLE I—*Continued*

Case and Year	Name	Sex	Age	Symptoms	Description	Pathology	Treatment	Living	Remarks
IV 1932	H	F	65	Bleeding 8 mo.	Tumor 2×3 cm. inside sphincter	Squamous cell epithelioma, Grade 3	High voltage roentgen therapy anus, 1600 r; radium—contact, 1 mm. gold filter, 1600 mg-hr.	Yes 7 yr.	Complains of tight sphincter
V 1934	R	M	65	Rectal prolapse 13 yr.—came on after a hemorrhoidectomy	Tumor 0.5 cm. anal mucous membrane	Squamous cell epithelioma, not graded	Radium-platinum needles interstitially around tumor, 1152 mg-hr.	Yes 5 yr.	Prolapse disappeared as a result of the radiation fibrosis
VI 1935	F	M	70	Itching around the anus with bleeding	Ulcer 1×2 cm. anal margin	Squamous cell epithelioma, not graded	Supervoltage roentgen therapy anus, 1800 r; gold radon seeds into tumor 933 mc-hr.	Yes 4 yr.	No complaints
VII 1935	M	M	77	Multiple discharging fistulae 10 yr.	Large, fungating infected tumor 12×15 cm. Large fixed nodes both groins	Squamous cell epithelioma, Grade 3	Supervoltage roentgen therapy: L. groin, 1800 r; R. groin, 1800 r; anus, 4200 r; radium-platinum needles, 1120 mg-hr.	No	Anal region cleared up. Died of general metastasis in 6 mo.
VIII 1935	D	M	44	Tumor for 4 mo.	Tumor 10×10 cm., fungating and ulcerating, occluding the anus	Squamous cell epithelioma, Grade 1	(1) Colostomy (2) High voltage roentgen therapy, anus, 3000 r	Yes 3½ yr.	Developed a radionecrosis over the coccyx which was removed and area healed. Well otherwise
IX 1936	K	F	52	Rectal bleeding and backache 4 mo.	Tumor 3×4 cm. ant. wall, extending into vaginal septum	Squamous cell epithelioma, Grade 3	Supervoltage roentgen therapy: 4200 r { anus 2700 r; coccyx 1500 r} Radium-platinum needles interstitially, 1120 mg-hr.	Yes 3½ yr.	No complaints
X 1937	L	M col.	51	Bleeding 1 yr., backache	Tumor 3×4 cm. inside sphincter on anterior wall	Squamous cell epithelioma, Grade 3	Supervoltage roentgen therapy: anus, 1800 r; L. groin, 900 r; R. groin, 900 r; radium-platinum needles, 2230 mg-hr.	Yes 1 yr. but failing	Patient developed internal metastasis. Very weak. Will die soon*
XI 1938	T	F	66	Bleeding 1 yr. and lump in anus	Tumor 3×3 cm. inside anus on posterior wall	Squamous cell epithelioma, Grade 4	Supervoltage roentgen therapy: 4200 r { anus 2100 r; coccyx 2100 r}	Yes 1 yr.	No complaints
XII 1938	P	F	73	Bleeding 1 yr., moderate pain	Cauliflower lump 6 cm. diameter protruding from anus	Squamous cell epithelioma, Grade 4	Supervoltage roentgen therapy: 4200 r anus: { 1st series 1800 r; 2nd series 1500 r; 3rd series 900 r} R. groin 1500 r L. groin 1500 r	Yes 1 yr. but failing	Tumor completely disappeared then recurred and invaded ischiorectal fossa. Developed metastasis internally*
XIII 1938	D	F	67	Bleeding 1 yr., pain in perineum	Mass 3×3 cm. in ant. wall, invading the perineum and vaginal septum	Squamous cell eptihelioma, Grade 3	Supervoltage roentgen therapy: 5400 r { anus 3600 r; sacrum and coccyx 1800 r} L. groin 1500 r R. groin 1500 r Radium—contact. 2 mm. gold; intrarectal, 600 mg-hr.; intravaginal, 600 mg-hr.	Yes 10 mo.	No complaints

* These patients have both died since the paper was read.

growth was on the mucous membrane side of the sphincters.

Pain was not a major symptom except late in the course of the disease and then only when the growth became so extensive that there was invasion of the deeper structures. Much of the pain was probably due to the accompanying secondary infection. An indefinite backache was present in 3 individuals, while only one had obstructive symptoms, though the anus seemed to be almost completely occluded in another.

How long the disease remains localized is difficult to answer. Given an area that is definitely and potentially infected—one that is constantly being compressed by the muscular contractions of both rectal sphincters—it would be only natural to expect dislodgment of tumor emboli into the lymph stream; however, these tumors are the fungating type and since they do not infitrate the base very early it is our impression that metastasis is rather late. Only 2 cases in this group had inguinal metastasis, while 2 others developed internal metastasis from one to two years after rectal bleeding first began. With such a slow natural course the outlook for successful treatment is favorable.

DIAGNOSIS

The diagnosis is not difficult. The examining finger can readily reach and should differentiate the normal from the abnormal. Excluding a papillitis and a thrombosed hemorrhoid, the only confusing conditions are the granulations encountered around old fistulous tracts. These may be pyogenic, tuberculous or luetic, and, in all, the clinical impressions must be verified by biopsy.

TREATMENT TECHNIQUE

All patients were treated by irradiation, but since the observation period extended over a fifteen year period, the technique as used varied considerably. The factors used were as follows:

I. *Roentgen Rays*
- (a) 200 kv., 4 ma., 0.5 mm. Cu plus 1 mm. Al, 50 cm. distance, 0.16 Å.
- (b) 600 kv., 4 ma., 0.8 mm. Pb, 50 cm. distance, 0.044 Å.

II. *Radium*
- (a) 50 mg., 1 mm. brass plus 1 mm. rubber filter
- (b) 50 mg., 2 mm. gold plus 2 mm. rubber filter

  } contact.
- (c) 1.3 to 2 mg. needles, filter 0.5 mm. platinum.
- (d) Radon seeds, filter 0.3 mm. gold.

Each case was individualized, the dosage varying according to the size of the lesion and histological structure. Usually roentgen therapy was given to the tumor through two portals: (*a*) the sacrococcygeal, (*b*) the anal or perineal. Treatment was given to the inguinal regions when metastases were already present or when metastases were suspected.

DISCUSSION

Since malignant disease of the anus is readily discovered by palpatory and visual examinations, it should be recognized early enough to be treated successfully either by surgery or irradiation. However, when radical surgery is the method of attack it has the disadvantage of removing or destroying the anal sphincters with subsequent loss of fecal control. On the other hand, when the operation is too conservative, local recurrence and inguinal metastases are prompt in their appearance. Since the tumors that have been graded have largely been either in Grade 3 or 4 of Broders' classification, one might expect recurrences.

Looking at the problem from a radiotherapeutic viewpoint, the great majority of these tumors are epitheliomata—types that have been successfully eradicated by irradiation in other parts of the body, so that the response here should be just as favorable. They are accessible and present little difficulty in administering an adequate tumor dose when treated by roentgen rays; while radium may easily be used in a contact applicator against the tumor,

or interstitially in platinum needles or as radon in gold seeds. Except for one patient who had a very extensive growth practically occluding the anus, there was no need for any supplementary procedure, as a colostomy. The discomfort from the treatment is not great and is a matter of three or four weeks. The patients are ambulatory and usually are able to care for themselves. The sphincter control has been good except in 2 patients, in both of whom the sphincter was partly destroyed by the growth itself; one had a colostomy and the other now complains of discomfort from a partial stricture following the treatment. Finally, the effectiveness of irradiation is shown in the eradication of the carcinoma for varying periods of time, as seen below:

Total cases reviewed	13	
Not treated	2	
Treated but dead	2	1 with advanced general metastasis at time of treatment
		1 moderately early who developed internal metastasis
Living	9	2—7 years
		1—5 years
		1—4 years
		2—3 years
		1—1 year (but failing gradually from internal metastasis)
		1—1 year
		1—less than a year

Though this series is small, it corroborates the opinion of Binkley and Bowing, who, from an extensive experience, emphasize the superiority of irradiation to surgery around the anus. Even such prominent rectal surgeons as Lockhart-Mummery and Rankin, who advocate radical surgery for carcinoma of the rectum, admit that irradiation is the method of choice in the treatment of epithelioma of the anus. Whether one should use roentgen rays or radium, combined or singly, is a matter of individual opinion and experience. We have combined the two methods, using roentgen irradiation first and following it with radium according to the individual response and need of each patient.

SUMMARY

Since cancer of the anus practically always belongs to the epithelioma group, its treatment by irradiation is the method of choice because:

(a) Histologically, it represents a type that responds readily and effectively to irradiation.

(b) The curability ranks on a par with surgery.

(c) The morbidity is low.

(d) Physiologic sphinter control is retained except where the sphincter is already partly destroyed by the disease.*

*For discussion see page 725.

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SURFACE APPLICATIONS OF RADON IN RECTAL CANCER*

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RADIUM and high voltage roentgen rays are of value in the treatment of rectal cancer. They may be used to advantage routinely in the inoperable stages of disease as a palliative method, and as a curative method in selected operable cases. The results to be obtained, in both the operable and inoperable groups, will depend largely upon the dose and technique of application. Due to variation in extent of the local disease at the time treatment is commenced, and variation in the grades of malignancy and radiosensitivity of rectal cancer, no uniform dose or technique of application is suitable for all cases.

The technique that has proved of greatest value in our clinic is the preliminary employment of external applications of radium or high voltage roentgen rays, supplemented by interstitial implantations or local surface applications of radon. External therapy exerts a favorable influence upon the tumor but this influence is not always sufficient, with the present-day technique, to provide the highest degree of palliation or to completely eradicate the disease. Gold filtered radon seeds, as a means of increasing the intensity of tumor dosage, were used routinely for many years; but during the past three years we have employed, in a number of cases, in place of interstitial applications, small daily surface doses of radon.

Treatment by local rectal applications of radium or radon is not a new method. It constituted one of the earliest attempts to influence rectal cancer by radium. The technique of application, in the early days, was rather inaccurate. Frequently, there was difficulty in placing the radium and retaining it in position. Doses were usually large, total doses being given in one, two or three large applications, at short intervals. Little attention was devoted to protection of the uninvaded rectal mucosa. Such local applications, at times, produced a favorable effect upon the cancer, but were frequently followed by a severe prolonged local reaction, characterized by marked tenesmus, burning, etc., which caused many patients to refuse further treatment. However, because of the favorable effect produced by this method upon the tumor in certain instances, it was decided to again use local applications, but to employ a different technique, giving careful consideration to the details which previously had produced undesirable local reactions.

Different types of applicators were tried. The type which has proved most satisfactory to date is one fashioned after an electrically lighted proctoscope. These scopes or tubes are slightly heavier than the ordinary proctoscope, the thickness being one-sixteenth of an inch of brass, which acts as a filter for the radium. The diameters vary from 1.5 to 2.5 cm., and the length from 10.0 to 25.0 cm. These applicators have a movable shoulder which may be fastened with a thumb-screw, so that the length of the tube inserted into the rectum is varied in accordance with the requirements of the case. This type of applicator can be adequately placed over the tumor by direct vision and fastened in position. The holders that contain the radon are modified obturators which fit within the applicators. The number of radon tubes for a given case are placed in the center of the distal end of the holder. By placing the radon in the center of the diameter, it is kept at a certain distance from the tumor. This distance will vary with the diameter of the instrument. The greater the diameter, the greater the tar-

* Read at the Twenty-fourth Annual Meeting, American Radium Society, St. Louis, Mo., May 15–16, 1939.

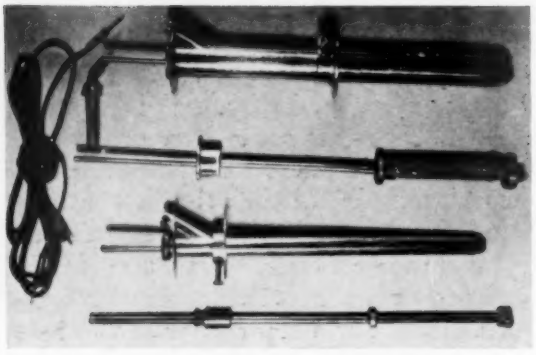

Fig. 1. Electrolighted rectal applicator and radium holders.

get distance and the greater the depth dose. Radon holders, in addition to containing radon, are fitted with lead shields to protect or provide additional filter for that part of the circumference of the rectum which is not invaded by cancer. Annular tumors do not require any shield. If the tumor involves less than one-third of the circumference a two-thirds shield is used. If less than one-half of the circumference is invaded, a shield of one-half size is used, etc.

Rectal applicator treatments are simple procedures and do not require hospitalization. Patients report for treatment daily. They are placed on a couch or bed in the left Sims' position. The applicator is inserted in a manner similar to that of passing an ordinary proctoscope. The instrument is passed above the tumor mass by direct vision, and then withdrawn so that the distal end of the scope is about 0.5 cm. above the upper limits. The radon holder, which previously has been loaded with the radon and the necessary shields, is inserted and fixed in position with a T-binder. The number of radon tubes placed in the holder will vary with the size of the tumor. These tubes, when arranged in tandem, should extend from 0.5 to 0.75 cm. above the upper limits of the tumor and the same distance below the lower limits of the mass. The length of radon in the holder may vary, therefore, from 3.0 to 12.0 cm. The time required for a treatment depends upon the amount of radon within the applicator and the size of the daily dose to be administered.

Dosage. It was quite evident, after treating a few cases by daily applications in the above fashion, that if reactions were to be avoided the daily doses must be small. After trying various amounts, it was thought that doses varying from 150 to 250 mc-hr. were most suitable as they could be continued for a considerable time. The selected dose depends somewhat upon the number of radon tubes used in the applicator. A small tumor which can be accurately covered by two or three tubes will usually tolerate from 125 to 175 mc-hr. daily. More tubes and larger doses are required to deliver a similar tumor dose to all cells of a larger tumor. A radon tube is about 1.5 cm. in length, and the dose that has proved most satisfactory varies from 30 to 60 mc. for each tube, keeping the total daily dose somewhere between 150 and 250 mc-hr. Daily and total doses are governed also by the diameter of the applicator. When the applicator is small, 1.5 cm. or less in diameter, the daily dose should be smaller than when the large sized applicator of 2.5 cm. is employed. Bougies, large catheters and small applicators in stenosing lesions produce but little growth restraint and have not been found of much value. The larger the diameter of the applicator, the more effective is the treatment.

Total doses will depend largely upon the size of the tumor, the number of radon tubes, the diameter of the applicator, the radiosensitivity of the cells and the object of treatment, whether for palliation or complete eradication. In the case of the small early favorable radiosensitive cancers, when only two or three radon tubes are necessary, the required total dose may not be more than 2,500 to 3,000 mc-hr. given in daily doses of 150 mc-hr. Cancers of a slightly larger size, and those of a more radioresistant nature, may require 150, 200 or 250 mc-hr. daily until the dose of 5,000 to 6,000 mc-hr., or more has been delivered. Careful observation as to re-

action and response of the tumor to treatment is of value in determining the total dose. If the response is not satisfactory after a moderate dose has been administered to an operable case, it may be advisable to use radon seeds or subject the patient to radical surgical removal. Total doses employed in the inoperable group have been smaller than those used with the object of eradication. The object of treatment in this group is to provide palliation without any additional upset or reaction to the patient. Therefore, it is wise to keep the dose within the limits of that which produces even mild reaction. Small daily doses, continued for periods of ten to fourteen days (total of 1,500 to 2,500 mc-hr.), usually produce very gratifying preliminary results. Occasionally much larger doses may be employed to advantage. Small series of treatments may be repeated in order to keep the growth under control. Small doses of gamma rays appear to have a marked influence upon the surface of the tumor characterized by a decrease of ulceration and infection and promoting a moderate degree of scar tissue, accompanied by a lessening of the local symptoms and an improvement in the general condition. Too large a total dose tends to produce breaking down on the surface and an increase of symptoms.

Untoward reactions following small daily doses of radon will be practically nil provided the cases are suitable for this type of therapy and that adequate dosage is employed. There were rather severe reactions in 2 patients with large squamous lesions. These reactions were characterized by severe pain and sloughing of the mass. The total dose in each case was large. We had a few moderate reactions in the early days of treatment in the inoperable group, by attempting to obtain a very high degree of palliation. There were 2 mildly painful skin reactions following treatments of lesions which involved the lower rectum and anal canal. In these 2 cases such reactions might have been avoided by a more careful placing of the radium. There has been very little post-irradiation damage to the surrounding rectal mucosa. In the operable group, there remains a small amount of scar tissue at the site of the original tumor in a few cases but in the majority little remains to indicate the site of the primary lesion. There has not occurred any degree of stricture formation worthy of mention from treatment of the early lesions. The majority of patients with small operable tumors felt better as soon as they had received four or five applications. Undesirable reactions in the inoperable group have been practically nil except in a few early cases where the total dose was too large.

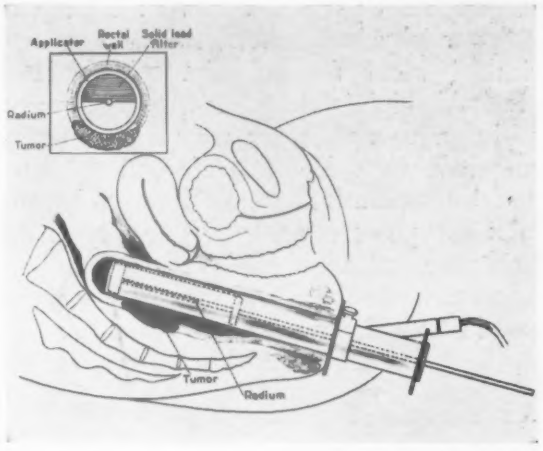

Fig. 2. Rectal applicator in position. Inset: Radium held in center of applicator, additional lead filter, one-half the diameter, to protect the normal mucosa.

Results. One hundred and nineteen patients were treated by this method prior to July, 1938. We were able to follow 114 of these patients for a sufficient time to draw some conclusions as to the value of the method. Eighty-one had advanced or inoperable disease. Thirty-three were considered, in accordance with the extent of local disease, to be operable cases. Thirteen of the operable group received this form of therapy prior to radical surgical removal, while 20 were treated with the object of clinical cure by radiation therapy, or a high degree of palliation. A fair percentage of patients with operable lesions chosen

for applicator treatment were elderly or in poor physical condition and not considered ideal for surgery. All patients received high voltage roentgen rays in addition to applicator treatments. While sufficient time has not elapsed to draw definite conclusions as to the final results of this type of treatment, a survey of the cases treated nine months or more ago offers a basis for advocating the method and continuing its use.

Results in the Inoperable Group. In the inoperable group of cases there appears to be additional palliation provided, other than that usually obtained from external irradiation, in about 90 per cent of the cases. In 30 per cent of these cases, the additional growth restraint and lessening of symptoms was mild. There appeared to be a moderate degree of additional effect in about 25 per cent of the cases. In the remaining 35 per cent there was a marked palliative effect. A large percentage of the latter group was rendered free of symptoms for a time. In comparing these palliative results with those obtained from the use of weak gold radon seeds in similar cases, in the majority of patients there appears to be an advantage in the local applications. However, gold seeds are still being used in cases that appear unsuitable for applicator treatment.

Small daily surface doses as a preoperative method of irradiation has a limited field. The chief limitation of this method is that the deep areas of infiltrating cells show little response. However, in some cases, there was a marked reduction in the size of the mass and considerable lessening of its fixation. In reviewing the pathological reports of 13 cases operated upon, there was a wide variation in the effect produced upon these tumors. In 2 cases, no evidence of cancer could be found. One of these was squamous cell and the other adenocarcinoma. Both cases had received very large total doses. In 8 tumors there were no recognizable changes that could be attributed to treatment. In the remaining 5 tumors the radiation changes varied a great deal.

The chief interest in this type of treatment has been with the small operable cancers, in an effort to provide clinical cures. The preliminary results in this small group are rather encouraging and suggest continuation of the method, but with careful selection of patients. Local applications have proved to be particularly suitable for the thin, small, radiosensitive lesions situated within the rectum proper or anal canal.

A review of the 20 operable cases treated by external irradiation and local applications, as a means of providing a high degree of palliation or complete eradication, shows the following results:

Two patients required operation, as the primary lesions failed to disappear. One patient, with a large, squamous cell cancer, has not been seen for six months, but is thought still to have the lesion. Local applications were supplemented with gold seeds in 2 cases. Both of these cases are considered clinical cures today. Two patients are dead. One, with squamous cell carcinoma, died with metastases to the liver but without local disease. The other patient was free of disease when last seen and the cause of death is unknown. One elderly woman has metastases to the liver. There was no local disease at her last visit. The remaining 12 patients, treated in the above manner, are alive and clinically free of disease for periods varying from one to three years.*

* For discussion see page 725.

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CARCINOMA OF THE COLON (EXCLUSIVE OF THE RECTUM)*

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CARCINOMA of the large bowel, excepting the rectum, is of course the most commonly encountered type of intestinal cancer. Most observers agree that the incidence of malignant degeneration of adenomatous polyps of the colon is approximately 50 per cent, though it has been stated to be as high as 85 per cent and as low as 18 per cent (Figs. 1, 2 and 3).

The reports vary with the histological interpretation of the polyp. Westhues has described an advanced change in these adenomas in which all order is lost. The branches, elongated tubules with cup-like outgrowths, the cells of which are many layered and deeply staining, have lost a definite relationship to the basement membrane. The muscularis mucosae is absent in many places and the connective tissue pedicle is sparse or absent. At the base of the lesion the gland tubules are distorted and pushed apart.

The papillomas comprise another gross division of benign polypoid tumors, and in histological examination of these tumors it is of importance to examine the whole

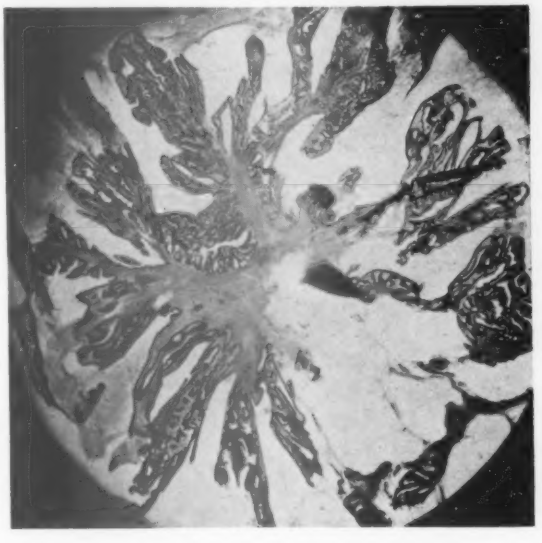

FIG. 1. Adenomatous polyp.

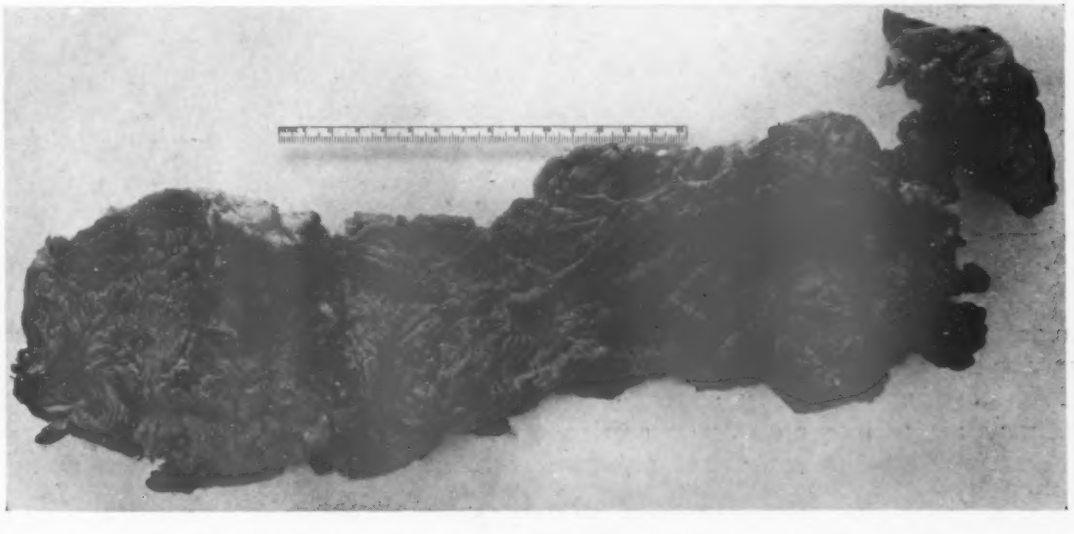

FIG. 2. Carcinoma at either end of a nest of adenomatous polyps. (Staff case, Palmer Memorial Hospital, courtesy of Dr. Richard Sweet.)

* Read at the Twenty-fourth Annual Meeting, American Radium Society, St. Louis, Mo., May 15–16, 1939.

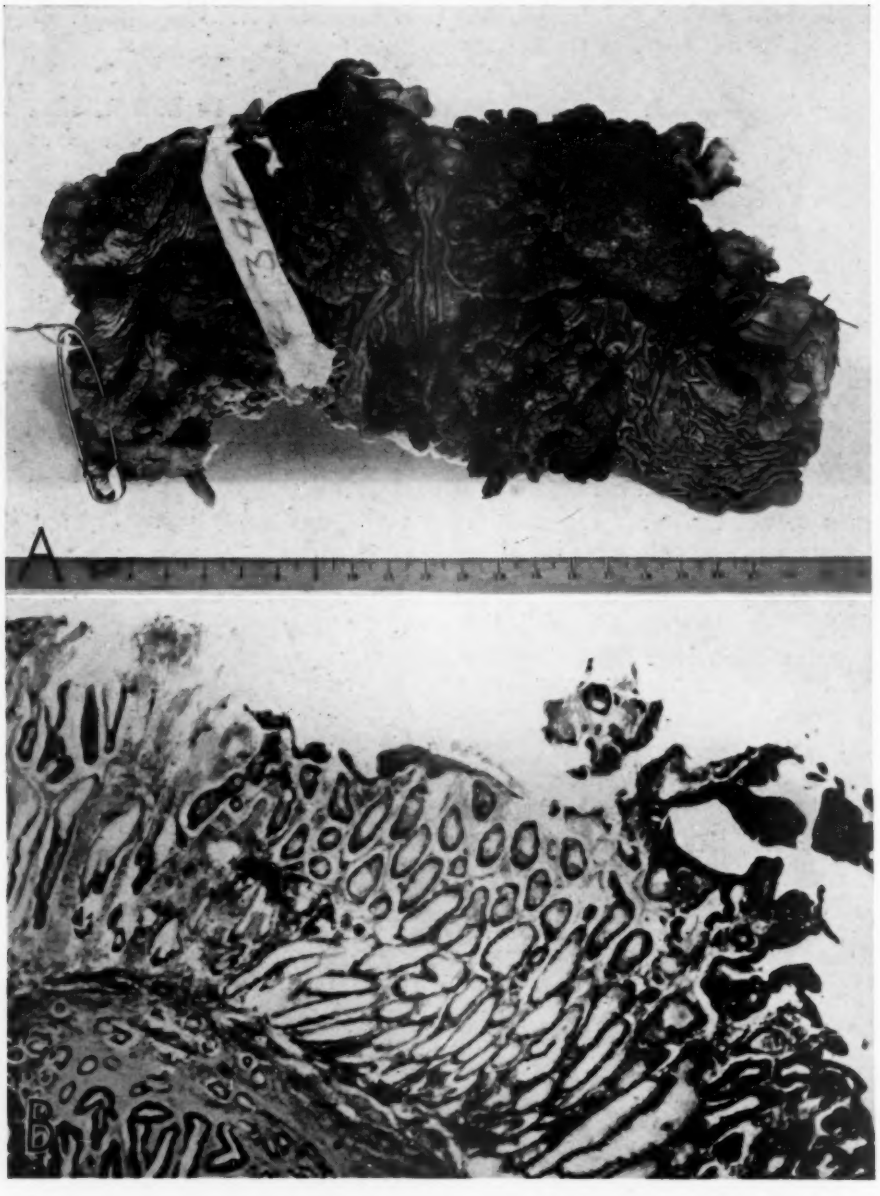

FIG. 3. *A*, two carcinomas of large bowel in close proximity, *B*, section of polyp which protruded from a colostomy.

tumor, as the base and center are most likely to show carcinomatous changes.

Multiple polyposis has an alarming tendency to carcinomatous degeneration. Several workers have demonstrated a gradual transition of polypoid growth from hyperplasia to adenoma with differentiated epithelial structure and then to less differentiated epithelial growths (Fig. 4).

It is not difficult to find instances of familial incidence of large bowel growths, both malignant and in the premalignant stage. As family histories are being more carefully investigated, an increasing number of instances of multiple polyposis, both with and without carcinomatous degeneration, are coming to light. This has been particularly noted in the literature of the past two or three years.

Both clinically and from the roentgen point of view, two definite types of growth

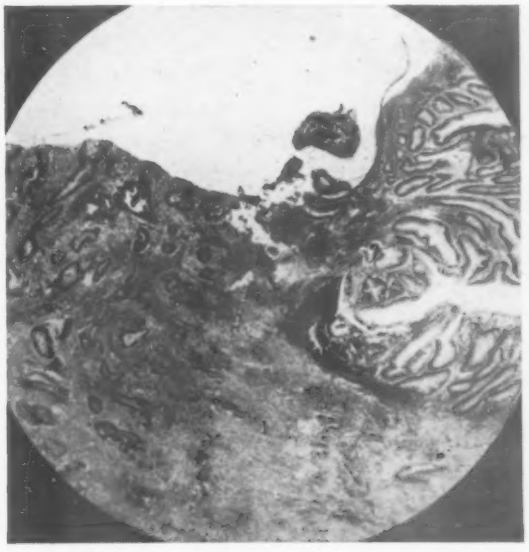

Fig. 4. Benign adenoma and adenocarcinoma in the same rectum.

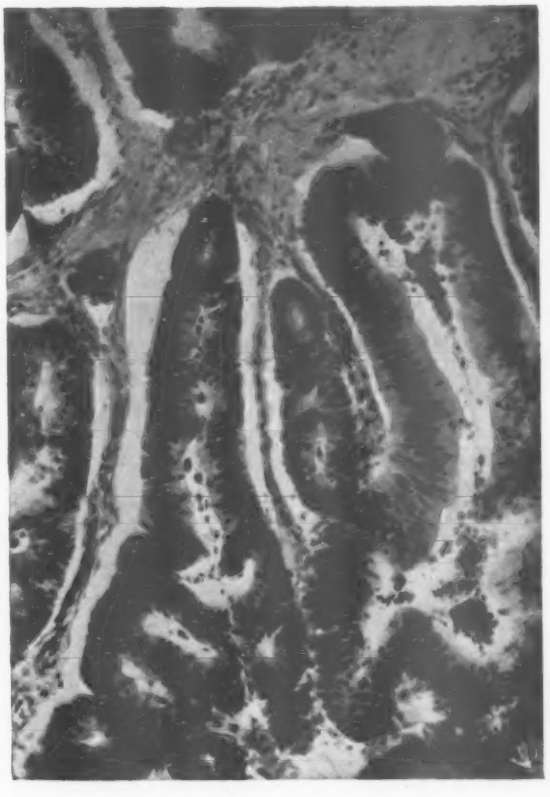

Fig. 5. Malignant adenoma.

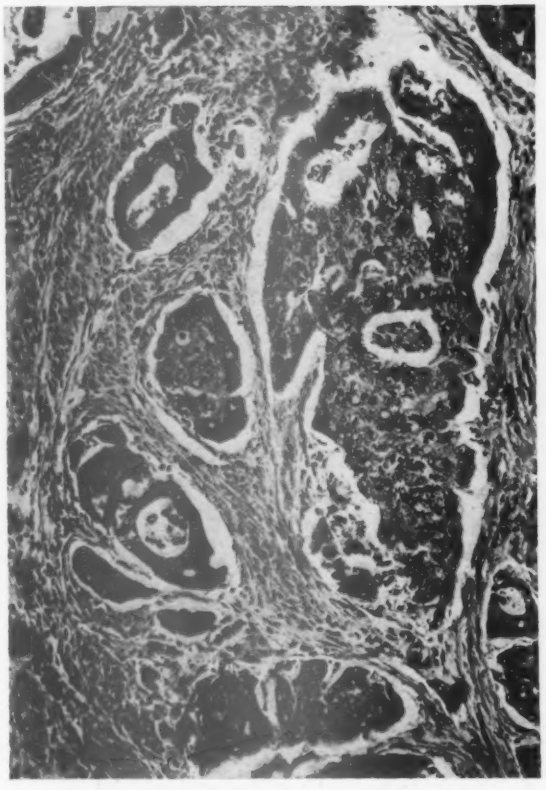

Fig. 6. Adenocarcinoma.

are recognized: (*a*) the medullary adenocarcinoma, commonly found in the ascending colon and at the hepatic flexure, and (*b*) the scirrhous obstructing type, usually seen in the remainder of the colon. This differentiation between medullary and scirrhous is often, however, only a gross one, for under the microscope the tumors of the two sides will many times not show this differentiation (Figs. 5, 6 and 7). Both have been found on either side of the colon, though the gross diagnosis in some instances of medullary or scirrhous carcinoma did not always coincide with the appearance under the microscope. Metastasis with carcinoma of the colon fortunately usually occurs late in the course of the disease. It must be remembered that enlarged hard regional nodes may not connote metastasis. We have in 2 cases recently resected a colon containing such nodes in the mesentery to find them entirely innocent of cancer.

SYMPTOMS

The symptoms are: (*a*) anemia, (*b*) intoxication, (*c*) obstruction.

Anemia: It is recognized that the medullary growths are friable and bleed easily. It has frequently been mentioned that the presence of this type of tumor in the right colon, that portion of the bowel which has a high capacity for absorption and where the fecal masses are still liquid, is a probable reason for the anemia and intoxication that are frequently seen in these cases. However, it is sometimes hard to explain the marked anemia and intoxication in cases with relatively small lesions. Recent studies have been made[4] of the intestine proximal to carcinoma of the right side of the colon, but no changes were noted in the anatomical structure of the intestine which might account for the associated anemia, on the basis of absorption of perverted substances. Obviously, absence of blood, either gross or microscopic, from the stools does not rule out cancer.

Obstruction: If obstruction supervenes, over three-quarters of the obstructing lesions will be found to be in the left half of the colon. While it is true that the right colon growth tends to grow in a centrifugal manner and is thus less likely to obstruct than its annular neighbor on the left, yet perhaps as good a reason for the tendency to bowel stoppage on the left is the diameter of the distal colon, which may normally be as small as 2.5 cm., as against 7.5 cm. on the right.

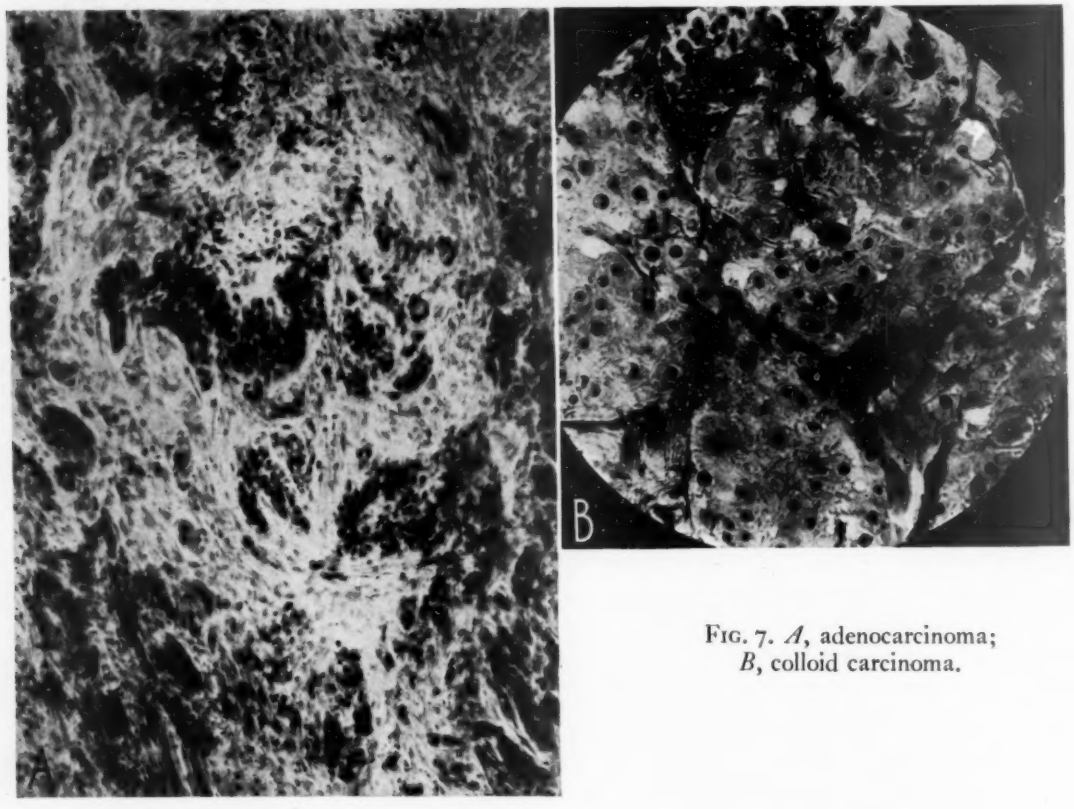

FIG. 7. *A*, adenocarcinoma; *B*, colloid carcinoma.

Fortunately these obstructive symptoms will often appear fairly early, but there is always the danger that the patient or the doctor will be misled by the disappearance of the vague slight symptoms of early obstruction after a change to a low residue diet or the ingestion of oil (Fig. 8). At the present writing, obstruction is being recognized clinically in about 50 per cent of the

cases. In about 5 per cent of these the obstruction is acute.

With the pressure of cancer publicity on both patient and doctor, more early cases are appearing. It is impressive to note the insignificance of the symptoms in these early cases. The patient may be so undisturbed by them that he only recalls them with an effort and often close questioning by the examiner. Only too often is it discovered that a minimal change in bowel habit, an insignificant digestive disturbance, a slight anemia or a vague slight general weakness indicate a process already quite advanced. There are still many carcinomas of the colon discovered first at autopsy.

The ideal situation would be, of course, one in which a carcinoma of the colon was treated before it had developed far enough to produce symptoms. Without question the more frequent employment of the barium enema as part of a routine physical examination will bring us nearer to attaining this end. As the barium enema examination becomes less expensive, more early cases will be discovered. We must keep always in mind that *there are no pathognomonic symptoms of carcinoma of the large bowel.*

Ten years ago we operated upon a carcinoma of the descending colon. In the eighth year following operation, the patient developed symptoms of pulmonary pathology which was diagnosed by the roentgen ray as carcinoma. But it was only at autopsy that the primary focus was discovered to be in the colon well above the level of previous resection—undiagnosed, for *it gave no symptoms.*

Fig. 8. Stricturing carcinoma. Symptoms relieved by injection of oil.

ROENTGENOLOGIC EXAMINATION

It is being increasingly emphasized that negative findings are of no significance, and there is a gratifying increase in accuracy in locating growths proximal to the sigmoidal flexure—in some series it is as high as 98 per cent. It is recognized that the opaque enema is not infallible and that lesions of the large intestine occasionally are present which give no roentgen evidence of their existence (Fig. 9). The contrast enema usually reveals those carcinomas which encircle the gut and produce some degree of stenosis. If, however, there is no constriction of the colon, the diagnosis may become difficult. The study of the mucosal pattern after evacuation of the contrast enema is of great importance and should be carried out in all cases, though the examination of the mucous membrane of the colon has not yet reached the degree of perfection that it has with gastric lesions. The combination of air insufflation and contrast enema is occasionally helpful, although of course it is

Fig. 9. *A*, carcinoma of the large bowel, roentgen examination negative after barium enema; *B*, after evacuation of barium.

not necessary to employ this method routinely. Care must be exercised in examining the flexures of the colon where overlapping loops are likely to obscure even well-advanced lesions (Figs. 10 and 11).

TREATMENT—SURGICAL

With cancer of the colon, particularly the right colon, the prospects of cure are usually better than with the stomach, as the lymphatic circulation is not so abundant. In the presence of obstruction, the ileus must obviously be treated first (Fig. 12). Preliminary colostomy markedly lessens the primary operative mortality. For removal of the tumor, four surgical methods are available:

(1) Excision of the growth with immediate anastomosis, preceded by several

Fig. 10. Loop of sigmoid conceals carcinoma proximal to it.

Fig. 11. Same patient as in Figure 10. Carcinoma of sigmoid revealed by pushing loop to one side.

Fig. 12. Flat plate showing intestinal obstruction.

days by a colostomy proximal to the growth. The following case history is illustrative.

W. K. S., aged fifty-seven, entered the hospital complaining of severe cramping lower abdominal pain. Duration three hours. Patient had had two similar attacks one month previously but they were so mild that he had thought nothing of them. Had no constipation in the interval between attacks. Barium enema quite negative and he was discharged. Ten days later he returned with a definite acute intestinal obstruction. An immediate cecostomy was done. Twelve days later the right colon was resected and an end-to-side anastomosis of the ileum to the hepatic flexure was performed. His recovery was uneventful.

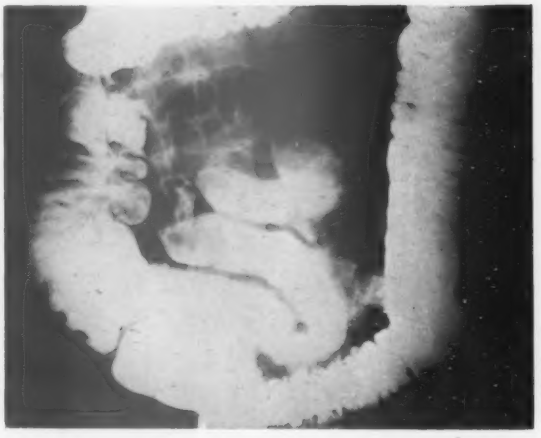

Fig. 14. Obstructing carcinoma of hepatic flexure.

Fig. 13. Carcinoma of the hepatic flexure.

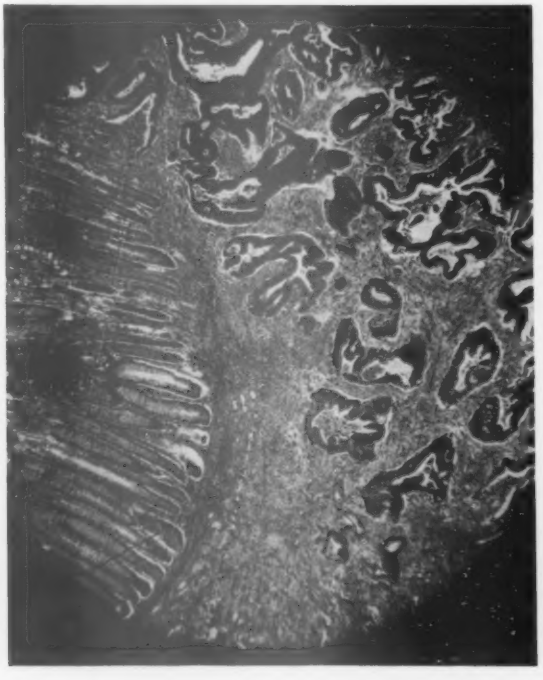

Fig. 15. Carcinoma of the hepatic flexure.

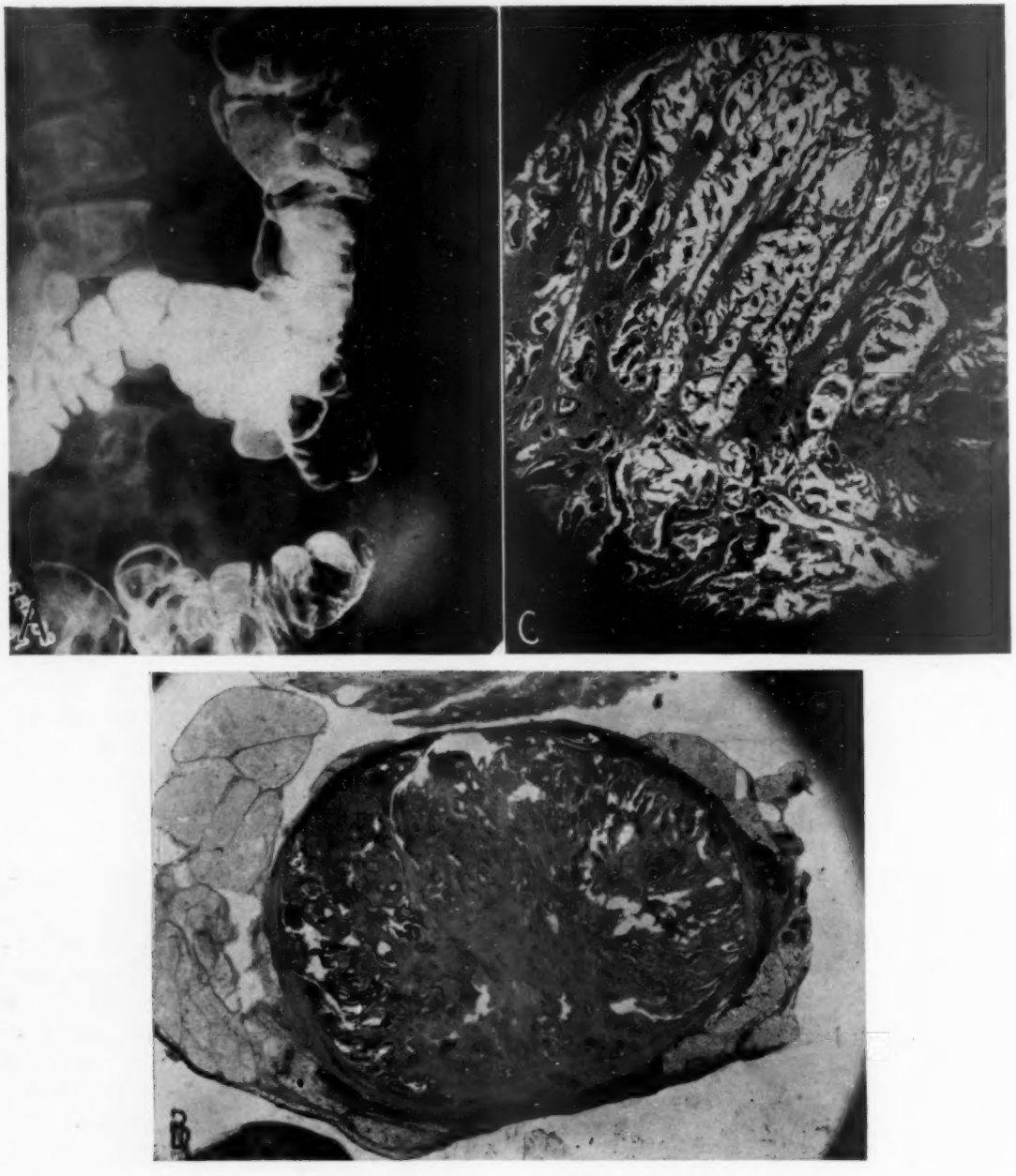

Fig. 16. *A*, carcinoma of descending colon. Excised by method of Mikulicz; *B*, carcinoma of descending colon. Node in mesentery; *C*, photomicrograph of section of carcinoma of descending colon.

Comment. Despite lack of constipation between attacks and a negative barium enema this patient had a constricting carcinoma of the hepatic flexure (Fig. 13).

(2) Preliminary anastomosis with secondary removal of the growth (in cases without obstruction) (Figs. 14 and 15). The following case history is illustrative.

W. W. G., aged sixty-seven, stated that one year and again six months before entrance he had a short attack of frequent loose stools without other symptoms. Between attacks bowels were quite regular. Began to lose weight three months before entrance and lost 7 pounds during that period. Appetite became poor during the same period. One week before entrance vomited and abdomen became distended, but

following this he had good results from an enema. He quieted down. This recurred the day before entrance. A cecostomy was done to relieve the obstruction. A barium enema showed a carcinoma of the hepatic flexure. Ten days later an ileo-transverse colostomy was performed. Two weeks later a right colectomy was done, including the cecum. No nodes were involved. The area of the cecostomy was drained. During convalescence a small superficial abscess was evacuated from the wound. Convalescence otherwise was uneventful.

Comment. Slow-growing carcinoma which probably could have been discovered several months earlier.

(3) Preliminary colostomy with secondary enterectomy followed eventually by closure of the colostomy. The following case history is illustrative.

J. B. McG., aged 65, entered the hospital because the constipation which he had noted for the past year had become more severe. He had no other symptoms. Barium enema showed an obstructing lesion in the descending colon. *Operation:* A transverse colostomy (at the proximal end of the transverse colon) was performed. His bowel distal to this point was well cleaned out during the next two weeks. A second operation was then performed. The involved descending colon with a goodly amount of accompanying mesentery was resected. Several large hard nodes in this mesentery were found to be merely inflammatory. At a third operation the colostomy was closed.

Comment. A preliminary colostomy was done because of beginning obstruction. A resection of a goodly amount of mesentery was performed because of palpable local nodes.

(4) The method of Mikulicz (Fig. 16*A*, *B* and *C*). The objection to this method is in the definite danger of transplantation of tumor cells into the abdominal incision. As high as 12 per cent has been reported. The obstructive resection of Rankin, when feasible, is a better operation. The operative mortality averaged over a number of series will be about 30 per cent. The mortality for lesions on the left side is always about 10 per cent higher than that with lesions of the right colon. The total mortality can be and has been brought as low as 12 per cent in large series. The following is an illustrative case history:

G. C., aged forty-five, stated that six months before entrance he had cramps just below the umbilicus. He was relieved as soon as gas was passed. Relieved by evacuation of bowels. No relation to meals. Has always been constipated, but with the use of oil and psyllium seeds his bowels became regular. No melena. No diarrhea. No loss of weight. At that time *abdominal examination* negative. An entrance examination revealed a mass, 6 cm. in diameter, along left flank at level of anterior spine of ilium. Barium enema showed an obstructive lesion of the descending colon. Resection (first-stage Mikulicz). Patient was then sent home for a month. During this time the spur softened and became more attenuated. At the end of a month the spur was crushed. One month later the colostomy was closed. Convalescence uneventful.

Comment. Inasmuch as at entrance the patient had a palpable fixed mass, it seemed questionably operable. However, resection was successful. Although nodes containing cancer were found in the mesentery, he has been well for over three years.

END-RESULTS

One should be able to attain approximately 50 per cent of three year arrests—but about one-quarter of these will recur after five years. However, Dixon has reported 55 per cent five year arrests with carcinoma of the cecum. The prognosis of carcinoma of the colon is increasingly less favorable as the more distal segments of the colon are involved. Lymphatic spread of right colon carcinoma commonly involves nodes in close proximity to the bowel. Resection of the affected segment, therefore, necessarily permits the removal of the accompanying lymphatic structures. The operability of carcinomas of the colon at the present writing is about 60 per cent.

The importance of obtaining material for microscopic examination either through a sigmoidoscope or a laparotomy cannot be overemphasized. The consequences which

may follow such an omission were forcibly brought to our attention a number of years ago in the case of a middle-aged man who developed symptoms of progressive intestinal obstruction. He was examined by barium enema and a complete arrest of the enema was noted at the recto-sigmoid junction. Exploratory laparotomy showed a large, firm mass involving the sigmoid which it was considered impossible to remove surgically. The patient was referred with a diagnosis of hopeless carcinoma. The obstructive symptoms had been relieved by cecostomy. Subsequent proctoscopic and roentgen investigations finally suggested that the mass was the result of diverticulitis. The patient was again explored and a permanent low left-sided colostomy was done. Seven years have elapsed and the patient is leading a normal existence, is in perfect health, and presents no evidence of malignant disease.

TREATMENT—RADIATION

The treatment of carcinoma of the large intestine with 200 kv. roentgen rays has given such discouraging results that we have practically discontinued this type of therapy. With the advent of supervoltage roentgen rays, however, it was felt that irradiation of malignant neoplasms of the colon should be resumed. Thus far, only a small group has been treated, consisting of 13 cases, 6 being low enough for sigmoidoscopic investigation. The entire group was hopeless from the surgical standpoint. These patients have been treated with the electrostatic belt-conveyor apparatus described in earlier communications. The following factors have been employed: 1,000,000 volts constant potential; 70 cm. distance; 3.5 mm. lead and 7 mm. copper filter; half-value layer 10.5 mm. copper; 70 r per minute, thimble-chamber air measurement. The daily doses ranged from 200 to 400 r, with total doses running as high as 6,000 r. We have been impressed with the tolerance which these patients have shown for supervoltage roentgen rays. Roentgen sickness has been definitely less than at lower voltages, and skin reactions have been negligible.

Radiation was administered as a palliative rather than a curative measure. These cases experienced relief from pain and diminution of bleeding. In several instances there was marked regression in the size of the growth. Two cases may be cited as examples:

A man, aged thirty-six, came under our observation a year ago with multiple large abdominal masses arising from a primary carcinoma of the sigmoid. The patient received two courses of supervoltage radiation, and at present there is no palpable evidence of disease other than slight thickening in the left lower quadrant. He is now symptom free.

The second case is that of a male, aged sixty-four, who in June, 1938, was found to have a carcinoma of the sigmoid which caused complete obstruction. A colostomy was performed. This patient has had five courses of supervoltage radiation with the result that a proctoscope now can be passed easily beyond the previously constricted area with no sign of ulceration or bleeding.

We appreciate that this group of cases of advanced, inoperable cancer has not been treated with any great enthusiasm and it seems likely that larger doses, which we have discovered are entirely safe to give, may lead to improved results.

SUMMARY AND CONCLUSIONS

1. Carcinoma of the colon is commonly encountered.

2. More early cases will be discovered if it is realized that they have no pathognomonic symptoms.

3. The benign adenoma, precursor of the malignant adenoma, must be diligently searched for, and destroyed.

4. A negative roentgen examination after a barium enema does not, of course, rule out carcinoma.

5. Resection of the involved bowel, preferably by stage operations, is the treatment of choice.

6. Palliation can occasionally be obtained with supervoltage radiation.

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DISCUSSION ON PAPERS OF DRS. MELAND, BINKLEY, AND SHEDDEN AND DRESSER

Dr. L. R. Sante, St. Louis, Mo. The question of anal, rectal and colon carcinoma again seems to me to revert to the question of type of cell and its radiosensitivity and the relative resistance of the normal surrounding tissue cells in which it is embedded. Frankly, the tumors in which we have had our success have been the ones in which there was the epidermoid type of carcinoma of the anus, and those that spread from posterior lip carcinoma of the cervix to involve the rectum.

It is obvious that since we do have success in those cases and have fewer successes in the adenocarcinoma types (the resistant cell types, which arise primarily from the rectum), this must be a matter, not so much of technique as the actual sensitivity of the cell.

I think rectal carcinoma is a bugbear for most of us and the matter of application is of course also of great importance. In this new applicator device as shown this morning it seems we have something very good. I think that in the past those of us engaged in general radiology and treatment have been rather remiss in our treatment of carcinoma of the rectum, feeling that there is nothing much we can do anyway, and we have by a more or less hit-or-miss method applied a rectal applicator, perhaps made up with radium tubes in an ordinary colon tube; or if the lesion were on one side, with one of the old-style fenestrated lead applicators with the radium in direct application to the tumor—with all of the lead on the opposite side for protection.

It seems to me the cylindrical applicator which allows for the increased distance is a great advantage. The application in this manner, of course, gives a greater depth dose and makes it easy to put in time after time.

I think the carrying of this matter of fractional dose radiation for the use of radium in rectal carcinoma and in the resistant type of cell structure is a very great advantage and it is a procedure that we should carry out with more exactitude and more frequently. It is a little bit difficult and it is quite a lot of inconvenience to get a patient up day after day and make a daily application of small doses of radium—it is quite a task, and I am afraid that many of us, on account of the disagreeableness of the task and the feeling of pessimism have not, perhaps, carried it out faithfully and given it the full amount of attention that we should.

I think that this applicator is certainly a great step in advance and it seems to me that it offers opportunities for different placement of radium rather than just the center of the applicator, because after all, this is not always the best or most advantageous arrangement for the radium.

In the use of seeds, it has always been very difficult for us to be sure that we are making any kind of a logical distribution of seeds in rectal carcinoma. Very frankly, it sounds easy, but when you look through a very small tube and there is a carcinoma high up and you see only the proximal end (it isn't always easy to visualize the other end to determine how far it extends), and above all you do not have the advantage of palpation, it is actually a very difficult thing to do.

Another troublesome complication which sometimes occurs and which leaves us fearful is the advent of a complication of perirectal abscess. I am sure that you have all had this condition develop after application of seeds at some time; it is an experience which causes one to err on the conservative side, in subsequent cases, resulting at times in insufficient irradiation of the growth.

I think utilization of the applicators that have been devised with careful thought in the individual case, maintaining the applicator in proper place, and the use of the fractional dose method, offer considerable advance in our treatment of carcinoma in this location.

In the matter of carcinoma of the colon, it seems to me that this is definitely the realm of surgery and our main function, if I may be permitted to say just a word in discussion of the paper that mentioned it, is in the early diagnosis of the lesion because in this place in the gastrointestinal tract there is an opportunity for early surgery to give very satisfactory results.

The insidiousness with which carcinoma hides around the bends of the colon was graphically demonstrated this morning, and how it is necessary to rotate the patient so as to uncover these bends in the rectosigmoid juncture, the hepatic and splenic flexures. If the constriction of the carcinoma is annular, the proximal dilatation of the colon—even if it is just a relative dilatation—and the distal constriction in itself points to the location of the lesion. But if it is pedunculated, springing from one wall so that it doesn't completely constrict the colon, then there is no dilatation above and the difficulty is greatly increased. It seems to me that we can help do our part by making an early diagnosis and being meticulous in our examination.

The application of roentgen therapy to such growths that may be large and inaccessible is of course just a palliative effort; we cannot view it with too great hope. If there is a colostomy with the colonic mucosa right next to the skin, both included in the roentgen field, and if the customary doses of radiation are given, you will see that very soon, before the skin shows any evidence of reaction, the intestinal mucosa will become definitely red, bleed, and will show a pseudo-membrane, and by the time actual reddening of the skin occurs there are already ulcerations of the colonic mucosa. This should in itself point out to us that the mucosa of the bowel is distinctly sensitive so that when it is involved with a carcinoma that is many times more resistant than the normal intestinal mucosa itself, we can have little hope of destroying the carcinoma without destroying the intestinal mucosa also. Therein lies the limitations of radiation therapy in the abdomen: the sensitiveness of the surrounding normal structures.

DR. ROBERT E. FRICKE, Rochester, Minn. It was my privilege last fall, at the meeting of the American Roentgen Ray Society, to hear and discuss Dr. Kaplan's paper on carcinoma of the anus. I believe the consensus at that time was that fortunately the incidence of this type of growth is rare and the treatment has to be highly individualized. The involved region is very tender both in regard to treatment and as regards the later reaction from the treatment. Although the primary growth "melts down" very swiftly and beautifully with treatment, and usually is a Grade 3 or 4 squamous cell epithelioma, the prognosis is always bad on account of the probability of later general metastasis.

Commenting on Dr. Binkley's paper, we have been using the surface treatment at the Mayo Clinic for many years, although our technique is a little different. We use two radon tubes strapped together, 50 or 60 mc. in each, introduced through a proctoscope with the patient on a Buie table and treat the different regions daily.

There are two groups of cases. In the larger group the treatment is only palliative as the patients already have metastases to the liver or lungs; one desires to control the distressing rectal symptoms and the dose is necessarily small. We give over each area about 50 to 100 mc-hr. per square centimeter a day until the lesion has been covered.

The other smaller group is made up of cases in which the lesion is operable. I believe there is quite a future for preoperative use of radium in these hopeful cases. Only a few are seen each year in our department. One year especially we studied results in a few cases in which radium therapy was used following colostomy in most cases during the convalescence from the colostomy. We treated the patients quite vigorously, and if we could get the surgeon to have patience for two or three months until the effect of treatment and the reaction from the treatment had been obtained, the subsequent posterior resection usually has been easier, the growths have practically always diminished in size and in 3 cases observed in one year there were no residual carcinoma cells found in the tissue removed at resection.

DR. MELAND (closing). I just wish to emphasize the fact that most of these patients that have epitheliomas of the anus are old patients. Even though they are technically operable, the surgical risk is great. Furthermore, those patients on whom we have done biopsies fall into the higher grades of malignancy, namely Grades 3 and 4. In irradiation we have a method of treatment that not only gives a high rate of curability but does not carry the mortality of radical surgery; while at the same time it preserves sphincter control.

Dr. Binkley (closing). I do not wish to be misunderstood or create the false impression that this method of applying radium is the ideal routine treatment for rectal cancer. It is only one of the many selective methods of treating this disease, most suitable as a curative method for early rectal cancer. Experience suggests that if patients come under observation in the very early stages, clinical cures can be brought about by this method without serious surgical operations or loss of sphincter control.

Radiation therapy in rectal cancer is of greatest value in two types of cases, i.e., early operable tumors and advanced operable stages of disease. The results of irradiation alone in advanced and medium-advanced operable stages are usually inferior to those following radical resection.

The radiosensitivity of the malignant cells is important in this form of treatment. Squamous cell cancers are more radiosensitive than the adenocarcinomas but this factor varies widely in both groups of cases. This method of application, with our present-day technique, does not appear suitable for eradicating the most radioresistant tumors, as demonstrated by the case which required operation after a very large dosage had been delivered.

The handling of radium for daily treatments over a long period of time presents a real problem. The danger has been greatly reduced by allowing one man to give the treatments for only one month during his period of internship. In order to help the intern during this period, and advise him as to details, patients are examined in the clinic once or twice a week to check the proper placing of the applicator and the reaction of the tumor to the treatment. The total dosages have been determined by this method of observation.

Dr. Shedden (closing). We feel that this small collection of hopeless cases was a sort of test group and that employing supervoltage roentgen therapy with them was distinctly worth while. The next step will be to apply the same type of treatment to a group of patients who are constitutionally inoperable but locally operable.

As regards the use of radium in cancer of the rectum, it will be found to be definitely more effective in combination with electrocoagulation than if employed alone. Moreover, the localization of the radium needles is easier on a base that has been electrocoagulated several days previously than the rather blind implantation into a bulky tumor.

CATHODE RAYS FOR RADIATION THERAPY

By J. G. TRUMP, Sc.D., R. J. VAN DE GRAAFF, PH.D., *and* R. W. CLOUD, S.M.
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THE possibility of using artificially accelerated high-energy electrons, or cathode rays, in radiation therapy has received occasional consideration.[1,2] Though medical use of cathode rays has not yet been made, considerable information on the biological effect of swift electrons is already available. The action of electrons has been observed to some extent in beta-ray therapy, for example, though beta rays are now rarely used because of the unfavorable character of the electron emission from naturally radioactive materials. Moreover, in roentgen-ray and gamma-ray therapy the biological effect is actually produced by the secondary electrons resulting from the absorption of photons within the tissue. Both roentgen rays and gamma rays thus serve in a sense simply as a means for accelerating within the tissue the electrons which are the actual therapeutic agents. The interest in cathode-ray therapy arises from the direct and advantageous manner in which the usual therapeutic agent—moving electrons—can be applied to malignant regions. It is the object of this paper to describe preliminary physical experiments made with cathode rays having energies up to 1,500 kilovolts, and to indicate from the point of view of physics some of the possibilities and techniques of cathode-ray therapy.

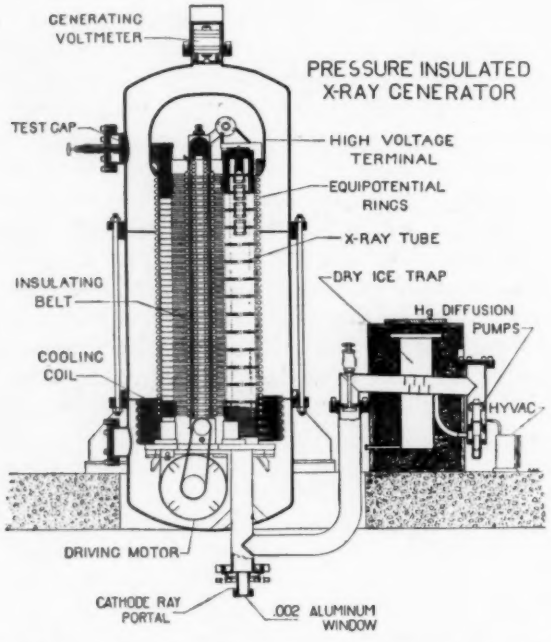

FIG. 1. Diagram of the pressure-insulated electrostatic roentgen-ray and cathode-ray generator.

CATHODE-RAY SOURCE

The cathode-ray beams used in this investigation were produced with apparatus developed primarily for 1,000 kv. roentgen therapy.[3] This roentgen-ray and cathode-ray source, which is illustrated in Figure 1, was developed at the Massachusetts Institute of Technology and will later be installed for roentgen therapy at the Massachusetts General Hospital. The high voltage generator and acceleration tube are enclosed in a steel tank within which air is maintained at a pressure of 10 atmospheres. This increased pressure is used to improve the voltage-insulating qualities of air and hence increase the compactness of the apparatus. The high voltage source is a constant potential, electrostatic generator in which electric charge is continuously transferred between a high voltage terminal and ground by a rapidly moving belt of insulating material. This terminal is spaced from the grounded steel tank so as to insulate the potential which it acquires due to the accumulated electric charge, and is supported by an insulating column of special construction along which the potential is accurately distributed by resistances. The acceleration tube is mounted vertically within the insulating column, the high voltage end

being inside the terminal. The electrons originate from a flat spiral tungsten filament at the high voltage end, and are progressively accelerated and focused as they pass down the tube by the multiple electrostatic lens system which derives its potential distribution from the column. At the grounded end this stream of electrons passes through a thin aluminum window and emerges from vacuum into air as a beam of electrons homogeneous in energy.

EFFECT OF HOMOGENEOUS AND PARALLEL CATHODE-RAY BEAM ON WOOD

When a beam of cathode rays, in which every electron has closely the same energy and direction as every other electron, is incident upon a block of wood, a qualitative impression of the distribution of the ionization energy within this material can be obtained from the charring effect produced. Figure 2 shows a section through a wood block after bombardment by a 1,500 kv. electron beam. It is seen that the zone of maximum energy absorption, or ionization, lies well below the surface, and that no evidence of ionization exists beyond a certain maximum depth which might be termed the range of electrons of this energy. The dosage which produced the charring effect in this sample of wood was approximately a thousand times a therapeutic dose. The time required to produce this charring effect could be selected at will by regulating the current in the beam. The time of irradiation can easily be made as long as several minutes in order to permit an accurate control of the dosage. The total amount of electric charge which is incident upon the material can be measured by the simple expedient of connecting an electrometer between it and ground.

DISTRIBUTION OF IONIZATION WITHIN VARIOUS ABSORBERS

Using the cathode-ray source described above, a study was made of the ionization produced by high speed electrons in their passage through lead, copper, aluminum, and water. The distribution of ionization in water is of special interest herein because of its close correspondence to tissue. The ionization was produced within a thin chamber mounted closely below the aluminum cathode-ray window. The electrodes of this ionization chamber, which is shown in Figure 3, consisted of a 0.0006 inch stretched aluminum diaphragm, insulated and separated by 0.030 inch from a heavy steel disk. By inserting between the cathode-ray window and this ionization chamber thin sheets of the material studied, the chamber could in effect be placed at varying distances below the surface of these materials and the ionization at these levels determined. For convenience, the material of the lower electrode of the ionization chamber was not changed to correspond to the absorber material, though this would be expected to have some effect on back-scattering.

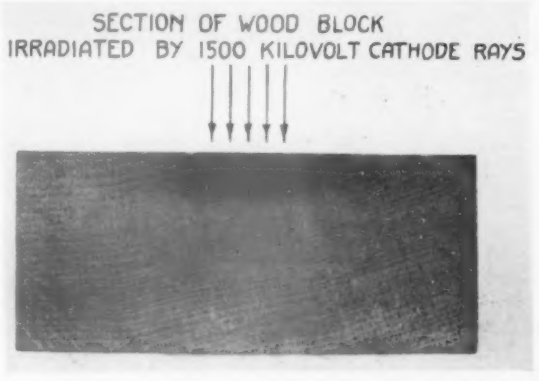

Fig. 2. Qualitative evidence of the distribution of the energy of a 1,500 kv. cathode-ray beam below the surface of a wooden block.

Measurements were made of the total electron current incident on the material, and of the ionization produced within the chamber for various positions below the absorber surface. The ratio of this ionization current to the incident electron beam current as a function of the thickness of the material interposed in the path of the cathode-ray beam is given in Figures 4 to 7 for lead, copper, aluminum and water,

respectively. These measurements were made with cathode rays incident with 300, 500, 900, 1,100, 1,300, and 1,500 kv. of energy. The minimum thickness interposed was in all cases the thickness of the cathode-ray window plus that of the ionization chamber diaphragm, and totaled 0.0025 inch of aluminum.

It is seen from the curves that for the cathode rays of higher energy the ionization at this closest position to the surface of the absorber is about 60 per cent of the maximum ionization. Examination of these curves also shows that the relative distance below the surface of the absorber material at which the ionization is a maximum is greater for materials of low atomic number—such as water—than for those of high atomic number. This characteristic, which is probably due to the effect of nuclear scattering, which increases with atomic number, is favorable to cathode-ray therapy, since tissue is composed primarily of elements of low number. The curves show that beyond the peak the ionization density falls steadily to a negligible value, indicating that the perceptible ionization effects are confined within the range of the electrons. This shows, as may be expected, that the roentgen rays produced by the cathode rays have no appreciable effect on the ionization density.

The range or maximum penetration of the cathode rays in the various absorber materials may be taken as the end points of the curves in Figures 4 to 7. The range in water has been plotted in Figure 8 against the incident energy in kilovolts. This curve shows a substantially linear increase in penetration with the voltage except at the lower values.

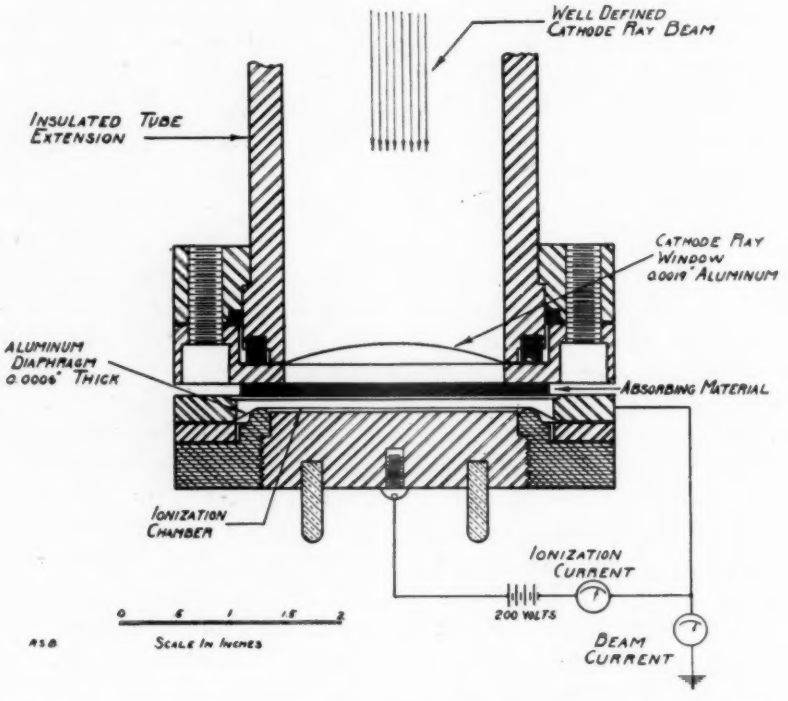

FIG. 3. Cathode-ray window and ionization chamber arrangement for the distribution of ionization measurements.

RADIATION THERAPY WITH CATHODE RAYS

The attractiveness of cathode rays for therapy lies in the fact that an ionization dose of therapeutic intensity can be applied to tissue in a fairly well localized region with only a fraction of the maximum

intensity at the skin and a negligible amount of ionization beyond the well-defined cathode-ray range. This is in marked contrast to the distribution of ionization found in roentgen therapy, in which ionization is maximum at the skin and proceeds to diminish in accordance with the absorption and inverse-square laws. Figure 9 compares the distribution of ionization produced by a parallel beam of 1,500 kv. electrons with that produced by a 100 kv. roentgen-ray beam used with a 20 cm. target-to-skin distance and 1 mm. aluminum filtration. The intensity of ionization at the skin is set to be the same in both cases. It is to be noted that more than 95 per cent of the total ionization produced by the cathode-ray beam lies within 7 mm. of the skin, though the maximum intensity is found well below the skin. With the roentgen-ray beam, on the other hand, though the intensity is highest at the skin, only about 12 per cent of the total ionization lies within the first 7 mm., the balance occurring in the underlying tissues. For superficial malignant neoplasms within the range of cathode rays, the enormously greater effectiveness with which the ionization can be applied with cathode rays may prove a factor of prime importance. In certain cases it may prove desirable to use roentgen rays and cathode rays in combination to secure the most favorable distribution of ionization.

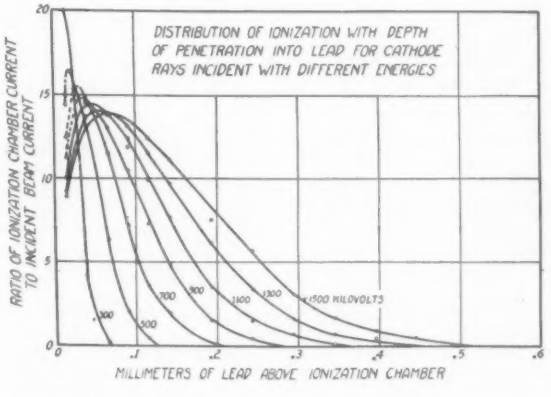
DISTRIBUTION OF IONIZATION WITH DEPTH OF PENETRATION INTO LEAD FOR CATHODE RAYS INCIDENT WITH DIFFERENT ENERGIES
RATIO OF IONIZATION CHAMBER CURRENT TO INCIDENT BEAM CURRENT
MILLIMETERS OF LEAD ABOVE IONIZATION CHAMBER
1,500 KILOVOLTS

Fig. 4. Distribution of ionization with depth of penetration into lead for cathode rays incident with different energies.

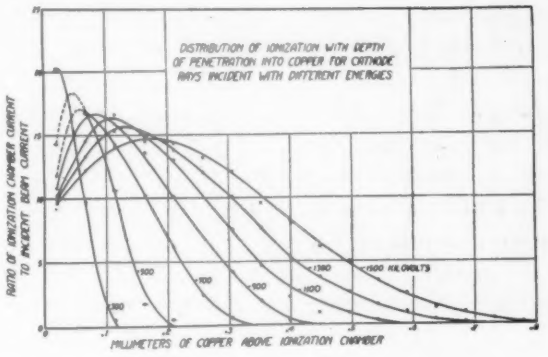
DISTRIBUTION OF IONIZATION WITH DEPTH OF PENETRATION INTO COPPER FOR CATHODE RAYS INCIDENT WITH DIFFERENT ENERGIES
RATIO OF IONIZATION CHAMBER CURRENT TO INCIDENT BEAM CURRENT
MILLIMETERS OF COPPER ABOVE IONIZATION CHAMBER
1,500 KILOVOLTS

Fig. 5. Distribution of ionization with depth of penetration into copper for cathode rays incident with different energies.

The present unavailability of cathode-ray sources for radiation therapy is due largely to the low range in tissue of even very high energy electrons. Only recently, using the highest constant potentials available, has the range of cathode rays become sufficient for the treatment of even very superficial malignant neoplasms. Fifteen hundred kilovolt cathode rays, as shown in Figure 8, have a maximum penetration of only about 7 mm. in tissue or water. Within this range is exhibited, however, the unique, localized distribution of ionization, the lack of which is one of the fundamentals limitations of roentgen therapy. For comparison with the 1,500 kv. cathode rays, the roentgen-ray voltage and

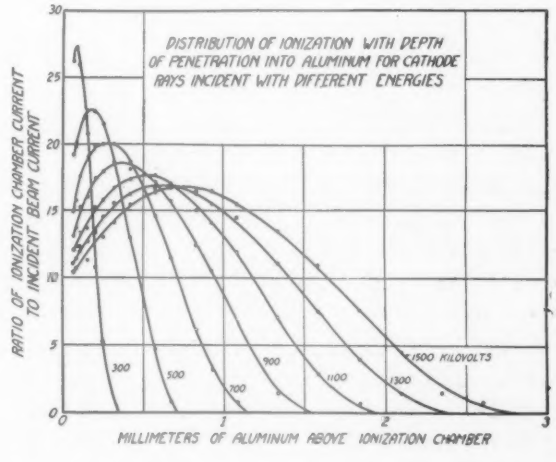
DISTRIBUTION OF IONIZATION WITH DEPTH OF PENETRATION INTO ALUMINUM FOR CATHODE RAYS INCIDENT WITH DIFFERENT ENERGIES
RATIO OF IONIZATION CHAMBER CURRENT TO INCIDENT BEAM CURRENT
MILLIMETERS OF ALUMINUM ABOVE IONIZATION CHAMBER
1,500 KILOVOLTS

Fig. 6. Distribution of ionization with depth of penetration into aluminum for cathode rays incident with different energies.

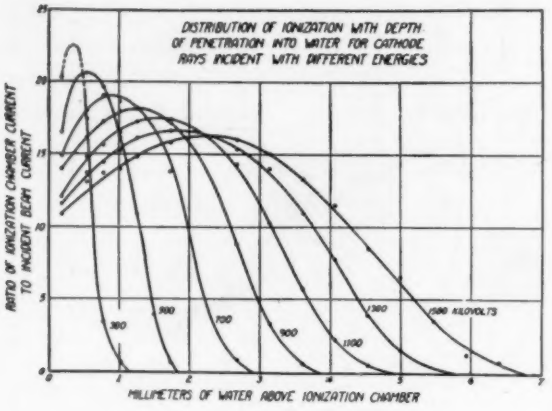

FIG. 7. Distribution of ionization with depth of penetration into water for cathode rays incident with different energies.

treatment distance used in Figure 9 was that typical of superficial roentgen treatment. Since the penetration of cathode rays increases directly with the accelerating voltage, developments now under way on the production of higher voltage sources may be expected to extend the present cathode-ray range several times. In the next few years, controlled beams of cathode rays homogeneous in energy and capable of penetrating several centimeters

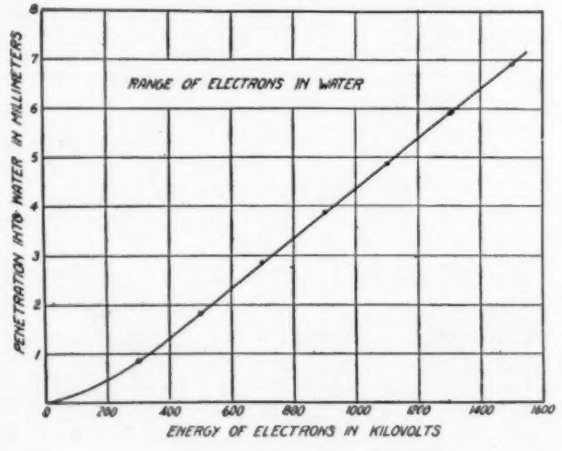

FIG. 8. Maximum range of cathode-ray beams in water as a function of their energy.

below the skin will probably become available for malignant growths within this range.

REQUIREMENTS FOR CATHODE RAYS USEFUL FOR THERAPY

The particular property of cathode rays which renders them of interest in radiation therapy lies in their manner of absorption, which permits the placing of well-localized dosages below the skin. This absorption characteristic is due to the fact that the individual electrons, like other high energy charged particles, produce their maximum ionization near the end of their path. Though the ionization is a maximum near the end of the path of individual electrons, the effect of scattering on a parallel beam of electrons homogeneous in energy is to

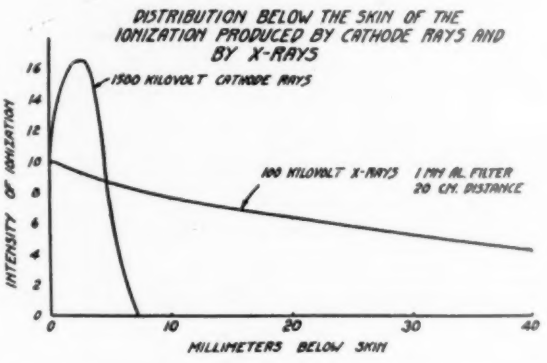
DISTRIBUTION BELOW THE SKIN OF THE IONIZATION PRODUCED BY CATHODE RAYS AND BY X-RAYS
1500 KILOVOLT CATHODE RAYS
100 KILOVOLT X-RAYS 1 MM AL. FILTER 20 CM. DISTANCE
INTENSITY OF IONIZATION
MILLIMETERS BELOW SKIN

FIG. 9. Experimental curves showing the distribution in material similar to tissue of the ionization produced by 1,500 kv. cathode rays and by 100 kv. roentgen rays.

move the region of maximum ionization nearer the surface. This is due, in part, to the fact that many of the electrons are deflected from the straight course within the absorber and hence have their maximum ionizing power nearer the surface. The effect of cathode rays not homogeneous in energy, but containing many particles of lower-than-the-maximum voltage, would similarly tend to bring the maximum intensity of ionization nearer the surface. The absorption curve for such cathode rays would not have, to nearly the same extent, the desirable characteristics of the curve illustrated in Figure 9. Hence it may be stated that the principal requirements of cathode-ray therapy, assuming suffi-

cient penetration, are that the rays be incident in a parallel beam essentially homogeneous in energy in order that the zone of maximum ionization may be localized and below the skin, and that the current in the cathode-ray beam be controllable so that the intensity of ionization may be of the same order of magnitude as that produced by roentgen rays in cancer therapy.

These requirements are not met by beta rays, which are not available in homogeneous or parallel beams of biologically useful intensity. Beta-ray emission from radioactive substances, as is well known, occurs with equal probability in all directions, and the distribution of energy among the emitted particles shows both a continuous and a line spectrum, with the lower energies predominating. The distribution of ionization about the beta-ray emitter, therefore, is strongly influenced by the inverse-square law and in addition shows high absorption immediately adjacent to the emitter surface. The net result is a region close to the emitter in which the radiation is excessive, beyond which the radiation rapidly diminishes to negligible proportions. This lack of control over the direction, energy distribution, and range of beta particles accounts for their disuse in radiation therapy.

The above requirements are also difficult to meet with cathode rays when a surge or a-c high voltage source is employed, due to the varying voltage and hence varying energies of the accelerated electrons, and also due to the lack of precise control of the electron current. With the constant potential electrostatic voltage source used in this investigation the voltage variation was of the order of 1 per cent, and the current in the cathode-ray beam could be regulated from a milliampere, which is used in roentgen-ray applications, to a very small fraction of a microampere, which would be desired for cathode-ray therapy. The particles in the cathode-ray beam could be sufficiently uniformly distributed over the desired area by placing a suitable scatterer some distance above the absorbing material and confining the beams by means of diaphragms to the area to be irradiated.

Intensity Needed in Cathode-Ray Therapy

Because of the directness of the cathode-ray process, less than one hundredth of 1 per cent of the current used in supervoltage roentgen therapy would be sufficient in cathode-ray therapy to produce comparable ionization intensities in tissue. In therapy with a million volt roentgen-ray generator[4] operating at about 1 milliampere, for example, the energy of the electron beam is converted into roentgen radiation at the target with an efficiency of a few per cent. Of this radiation about 1 per cent passes through the roentgen-ray portal toward the patient. The ionization directed at the patient represents, therefore, a few hundredths of 1 per cent of the energy in the electron beam, and of this only a small fraction is absorbed within the tumor. In cathode-ray therapy, on the other hand, all of the electron energy within the prescribed beam area would be incident on the patient, and its effect would be localized within the limited range of the electrons. In order to produce within this localized region an ionization by cathode rays which is comparable in intensity to the ionization produced by roentgen rays in a typical treatment, the cathode-ray current should thus be less than one-tenth of a microampere. Such a controlled beam current, which is easily obtained with a constant potential voltage source, could be expected to produce its therapeutic effect at substantially the same rate as that now observed with roentgen rays. Since in roentgen therapy the therapeutic agents are the secondary electrons accelerated by the absorbed and scattered roentgen-ray quanta within the tissue, it is evident that the biological effect would in both types of therapy be due to moving electrons.

It is one of the advantages of homogeneous and parallel cathode-ray beams such as would be used in therapy that they can be described in a more simple and exact manner than roentgen-ray beams. Such incident cathode radiation is described by specifying the voltage, current, and treatment area. The character of an incident roentgen-ray beam, on the other hand, depends in addition to these factors on the wave form, target material, filtration, radiation angle, and treatment distance.

RANGE OF CATHODE RAYS IN TISSUE

With the 1,500 kv. cathode rays obtained with the present apparatus, the maximum range in water—and therefore in tissue—is about 7 millimeters. This present range is sufficient for exploring some of the biological effects of cathode rays and may later prove of medical interest in the treatment of certain types of very superficial malignant conditions. While many of these can already be effectively treated with roentgen rays, except when the involved area is large, the advantage of lower skin damage, of the higher intensity at the inner region of the malignant neoplasm, and of the absence of destructive action beyond the well-defined range of the electrons may prove significant. It is to be expected also that in the future substantial voltage increases will be made so that the penetration of cathode rays can be gradually extended to more deep-seated malignant tumors.

The authors take pleasure in expressing their appreciation of the generous grant of the Godfrey M. Hyams Trust which made possible the development of the pressure-insulated roentgen-ray and cathode-ray generator used in this investigation. They also wish to acknowledge the able assistance of Augustus T. Norton, Jr. in this work.

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A COMPARATIVE ROENTGEN-RAY DIFFRACTION STUDY OF SEVERAL NATURAL APATITES AND THE APATITE-LIKE CONSTITUENT OF BONE AND TOOTH SUBSTANCE*

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THE roentgen-ray diffraction evidence concerning the structure of the inorganic constituents of bone and tooth substance has consisted largely of the repeated observation that the powder diffraction patterns of these substances are similiar to that of fluorapatite. It had been suggested previously that bone and tooth substance was isomorphous with the mineral apatite from the results of chemical studies[1] and from observations with polarized light.[2] Since tooth and bone substance contain little fluorine and considerable amounts of carbon it has been supposed by some that they are essentially carbonate apatites, with carbonate ions replacing the fluorine in the apatite structure.

Quantitative data concerning the variations in the structure of tooth and bone substance from that of fluorapatite are quite meager. Two independent determinations of the structure of apatite itself have been published. They are similar except that St. Náray-Szabó[3] places the fluorine ions at the $00\frac{1}{4}$, $00\frac{3}{4}$ positions of the unit cell, while Mehmel[4] gives their position as 000, $00\frac{1}{2}$. Hendricks, Jefferson and Mosley[5] have measured the unit cell dimensions of bone and related substances. They state that florapatite, hydroxylapatite, oxyapatite, tricalcium phosphate hydrate and bone all have different diffraction patterns and can be thus identified. From packing considerations, they suggest a structure for bone as a carbonateapatite hydrate. Klement and Trömel[6] deny the existence of oxyapatite and tricalcium phosphate hydrate as crystalline entities, and state that the diffraction pattern of bone is the same as hydroxylapatite and that therefore bone is essentially hydroxylapatite. Hodge, LeFevre and Bale,[7] and Thewlis, Glock and Murray,[8] among others, have also concluded that tooth and bone substance are essentially hydroxylapatites. Reynolds, Corrigan, Hayden, Macy and Hunscher[9], state that the diffraction pattern of calcium fluoride appears along with that of hydroxylapatite in the teeth of rats fed excessive amounts of fluorine. Reynolds, Hayden and Corrigan[10] repeat that bone from a case of hyperthyroidism showed a diffraction pattern different from apatite. In all cases, with the exception of St. Náray-Szabó's apatite determination, intensity measurements have been limited to visual determinations from diffraction photographs. It is therefore difficult to judge between conflicting reports as to whether two substances do or do not give equivalent diffraction patterns. Due to this lack of quantitative experimental data, the only statement that can be made with certainty from roentgen-ray diffraction data is that tooth and bone substance is largely an apatite-like material.

It seemed therefore worth while to measure quantitatively the diffraction spectra of these related substances in an effort to make the present knowledge concerning the structure of tooth and bone substance more precise. Long radius cassettes, a Bragg type ionization spectrometer suitable for either single crystal or powder spectra measurements, and a powder spectrometer utilizing a Geiger-Müller counter as a suitable detector for weak diffraction maxima, were used in obtaining these data.

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EXPERIMENTAL DATA (PHOTOGRAPHIC)

A total of thirty-five natural apatites or minerals supposedly resembling apatite in structure has been studied by roentgen-ray diffraction methods.* The roentgen-ray diffraction patterns of eighteen out of twenty minerals described as fluorapatites from widely distributed points of the world and in many cases of widely varying appearance are apparently identical. The diffraction patterns of two others of the fluorapatite samples were identical with these except that there were superimposed patterns of obvious mineral impurities. Collophanite from the island of Mona (described as monite) has a fluorapatite diffraction pattern. Other collophanites (described as pebble rock phosphate) have a diffraction pattern entirely dissimilar to that of apatite. Of special interest were several apatite-family minerals reported as containing considerable amounts of carbonate, and often described as calcium carbonate phosphates. Of these minerals, two specimens described as dahllite, and one specimen described as francolite gave distorted apatite-like diffraction patterns, considerably different from fluorapatite, however, both as to line positions and intensities. Three specimens of staffelite from different localities, one specimen of osteolite, and one specimen of koprolite gave diffraction patterns indistinguishable from fluorapatite.

Powdered bone substances, dentine, and enamel give diffraction patterns which, both as to line positions and intensity, are very similar to diffraction patterns of fluorapatite. Small, but definite and consistent differences do exist, however, as to line positions and comparative intensities. Tooth and bone substance, and fluorapatite are much more alike than either is to any of the other apatite-like diffraction patterns previously mentioned.

The preferential crystal orientation that is present in intact enamel, and which accounts for its distinctive diffraction pattern, has been described adequately by Thewlis[11] and by Bale and Hodge[12] elsewhere. The diffraction pattern of powdered tooth enamel (in 17 separate samples and 200 different pictures) has always been that of an apatite-like substance with characteristics and constant deviations from fluorapatite. The diffraction pattern of powdered enamel is sharp and precise with a background of general scattering nearly as low as powdered apatite. The diffaction maxima, however, appear slightly broader than those of apatite taken under similar conditions of high resolution. There has never been any evidence of grain in the diffraction picture due to crystals of appreciable size in the enamel. Single approximately homogeneous crystals are therefore always very small. Size estimates have been published elsewhere.[13]

Dentine and the inorganic portion of bone substance give similar diffraction patterns distinguished by broader and more diffuse intensity maxima than is characteristic of enamel. Dentine, when untreated except for powdering, has a much greater background of generalized scattering than enamel. This background is appreciably decreased but still much greater than enamel when the organic material is extracted from dentine by the glycol ash method described by LeFevre, Bale and Hodge.[14] When starch is mixed with enamel in proportions to produce about the same amount of generalized scattering as is present in dentine, many of the fainter enamel lines are still distinguishable. These lines are not visible in dentine (or bone) even though the principal dentines may be more intense than the corresponding ones of enamel. Except for these differences ascribable to small crystal size, the diffraction patterns of dentine and bone substance are the same as those produced by tooth enamel. The same features are present in the diffraction pattern of bone and dentine that distinguish enamel from fluorapatite, and more noticeably from the other apatite-like natural minerals.

* All natural minerals were obtained from Ward's Natural Science Establishment, Rochester, N. Y

In connection with a chemical study, diffraction patterns of a large number of primary, secondary, and tertiary calcium phosphates as well as hydroxylapatites were prepared. The detailed results of this work are reported elsewhere[7] and only those results will be described here that are directly pertinent to the structure of teeth and bone. The tricalcium phosphates examined gave in each case diffraction patterns that were either, so far as could be told by visual examination, the same as the diffraction pattern of tooth and bone substance or consisted of this diffraction pattern and superimposed upon it the diffraction pattern of one of the modifications of secondary calcium phosphate. The diffraction maxima of these tricalcium phosphates were more diffuse than the diffraction maxima of enamel. Hydroxylapatites have diffraction patterns also indistinguishable from those of dentine and bone, with the exception that the diffraction maxima were usually more sharp; often they were indistinguishable from tooth enamel. By contrast, certain of the tricalcium phosphates gave diffraction patterns so diffuse that they had almost the appearance of the diffraction patterns of liquid or amorphous substances.

On ignition at 900° C. the diffraction pattern of fluorapatite is unchanged. The effect of ignition on the higher calcium phosphates[10] depends upon both the calcium-phosphate ratio and the mode of preparation. On igniting samples with the theoretical chemical composition of tricalcium phosphate and precipitated by adding calcium ions to phosphate, a distinctive pattern called β tricalcium phosphate[15] is produced. Samples with the theoretical composition of hydroxyapatite, precipitated by adding phosphate to calcium, on ignition showed only the unignited pattern with a further sharpening of the diffraction maxima.

In enamel there was no very evident change on ignition. There is some sharpening and increase in intensity of the weaker diffraction maxima.

On igniting dentine three different results have been obtained: (1) in most cases there has been only a sharpening of the diffraction maxima to an appearance similar to that of enamel; (2) certain specimens[16] have undergone a partial change to the $\beta Ca_3(PO_4)_2$ pattern; (3) in certain instances, there has been an increase in the c-dimension of the unit cell which results in a diffraction pattern resembling that of chlorapatite. This pattern has been duplicated by igniting $Ca_3(PO_4)_2$ plus calcium chloride in amounts theoretical for chlorapatite.

A study of tooth sections using the pinhole diffraction method showed no change in the enamel pattern after ignition, either in the material present or in the preferential orientation of the crystalline constituent. Small change in the nature of the diffraction pattern would not have been detected by this method, due to the large and variable changes from the normal pattern caused by the preferential crystal orientation.

QUANTITATIVE INTENSITY DATA

The ionization spectrometer was used to study the powder diffraction spectra of enamel and fluorapatite quite extensively, and to make less elaborate measurements on the diffraction patterns of dentine, bone, ignited enamel and the various available hydroxylapatite and tricalcium phosphate samples. Mo Kα radiation filtered through zirconium oxide was used in every case. Three different methods of holding the diffracting sample could be utilized permitting (*a*) reflection from a surface, (*b*) transmission through a powder cake of uniform thickness with the incidence beam at the Bragg angle from the normal, and (*c*) transmission through a round thin-walled glass tube filled with the substance being examined. The data presented in Figures 1 and 2 were obtained by the third method. With the narrow slit system used, experiments showed that, with angles up to 20 degrees, this method closely approximated transmission through a slab of uniform thickness.

Figure 1, *a*, represents the diffraction pattern of fluorapatite as determined by the roentgen-ray spectrometer. The lower curve (Fig. 1, *b*) represents the same diffraction pattern with the background of general scattering removed as well as possible by graphical analysis. Figure 2, *a* and *b*, shows the corresponding data for tooth enamel. Other experiments utilizing the ionization spectrometer, the powder spectrometer equipped with Geiger-Müller counter, densitometric records, and visual inspection, show that both these records are acceptable as typical intensity measurements of the diffraction patterns. The great similarity in the diffraction spectra of the tooth enamel and fluorapatite is evident, as are also the variations, mainly quite small, of positions and of relative intensities of corresponding diffraction maxima.

It has been stated[6,17] that the diffraction pattern and therefore presumably the unit cell of tooth and bone substance and of hydroxylapatite are identical, and that oxyapatite and tricalcium phosphate hydrate do not exist as crystalline entities.[6,18] Other investigators,[5] however, have stated that hydroxylapatite, tricalcium phosphate hydrate, oxyapatite and bone give sufficiently different diffraction patterns so that these substances may be recognized from their characteristic pattern. The latter reports have also given

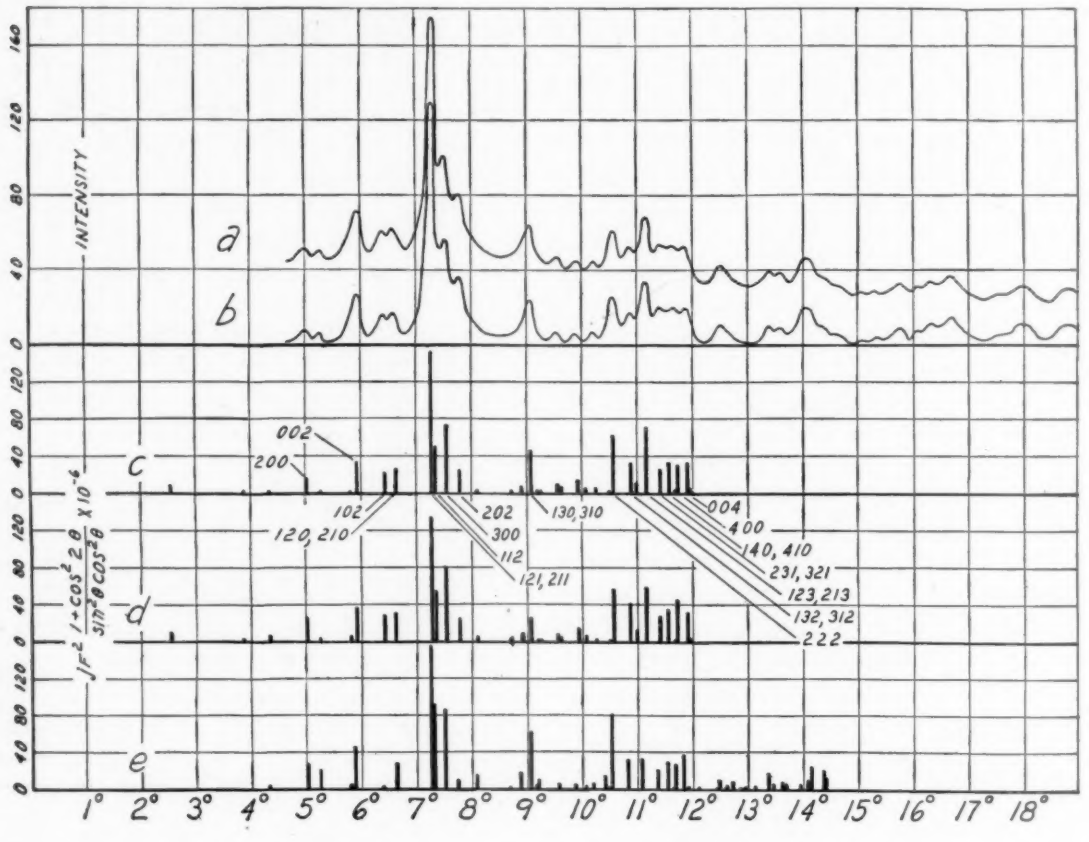

Fig. 1. Fluorapatite diffraction data. *a* represents the powder diffraction spectra of apatite as measured with the ionization spectrometer, plotted with ionization intensity as ordinate and θ as abscissa. *b* is the same as *a* except that the background of general scattering has been removed graphically. *c* is the diffraction spectra calculated from the apatite structure proposed in this paper. *d* is the diffraction spectra calculated from St. Náray-Szabó's proposed apatite structure. *e* is the diffraction spectra predicted by St. Náray-Szabó's calculated F-values for apatite.

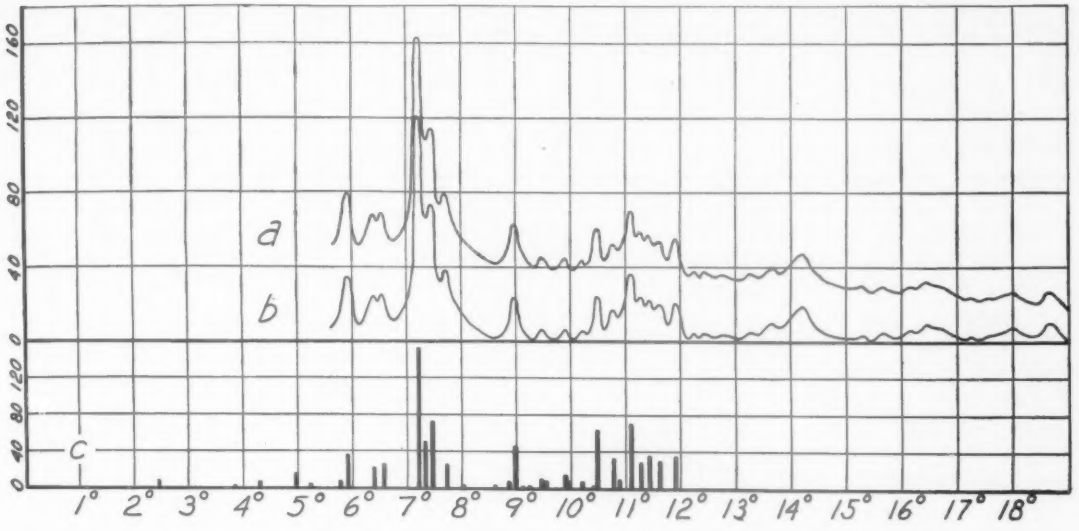

Fig. 2. Tooth enamel diffraction data. *a* represents the powder diffraction spectra of tooth enamel as measured with the ionization spectrometer, plotted with ionization intensity as ordinate and θ as abscissa. *b* is the same as *a* except that the background of general scattering has been removed graphically. *c* represents the diffraction spectra of apatite as calculated from the fluorapatite structure proposed in this paper with the exception that the diffraction angles used are those of tooth enamel rather than of apatite.

measurements for these substances (recorded in Table 1) of unit cell dimensions which differ among themselves in some cases by several times the experimental error. Because of this conflicting evidence it seemed wise to measure these different units as accurately as possible.

The powdered substance being studied was held in a thin-walled, glass tube. For calibration and also to eliminate errors due to absorption or to variations in the physical set-up of the various experiments, a mixture of either NaCl or of SiO_2 and the substances being studied were used. The criterion for designating a given sample as tricalcium phosphate hydrate was that on ignition at 900° C. it should be entirely transformed into β tricalcium phosphate. Similarly the criterion for hydroxylapatite was that the diffraction pattern should be heat stable at 900° C.

For the measurement of the a-dimension of the unit cell the 130 plane diffraction maxima were used, since it is well separated from confusing lines. For the c-dimension, measurements of 002 and 004 maxima were made. Figure 3 shows typical experimental data for each of these sub-

Table I

UNIT CELL DIMENSIONS OF SOME APATITE-LIKE SUBSTANCES

	Previously Reported Values		Present Values	
	a	c	a	c
Apatite	9.37 ± .01	6.88 ± .01	9.37 ± .02	6.88 ± .02
Bone	9.27 ± .03	6.95 ± .03	9.48 ± .04	6.88 ± .04
Tooth enamel			9.47 ± .03	6.88 ± .03
Hydroxylapatite	9.40 ± .03	6.93 ± .03	9.47 ± .03	6.88 ± .03
Oxyapatite and ignited bone	9.38 ± .03	6.93 ± .03	9.47 ± .03	6.88 ± .03
Tricalcium phosphate hydrate	9.25 ± .03	6.88 ± .03	9.47 ± .05	6.88 ± .05

The previously reported values for apatite given above are those of St. Náray-Szabó.[3] The values for the other substances are those given by Hendricks, Jefferson and Mosley.[5] Thewlis, Glock and Murray[6] have published values for apatite, tooth enamel, and hydroxylapatite that within the reported experimental error are in agreement with the results of the present authors.

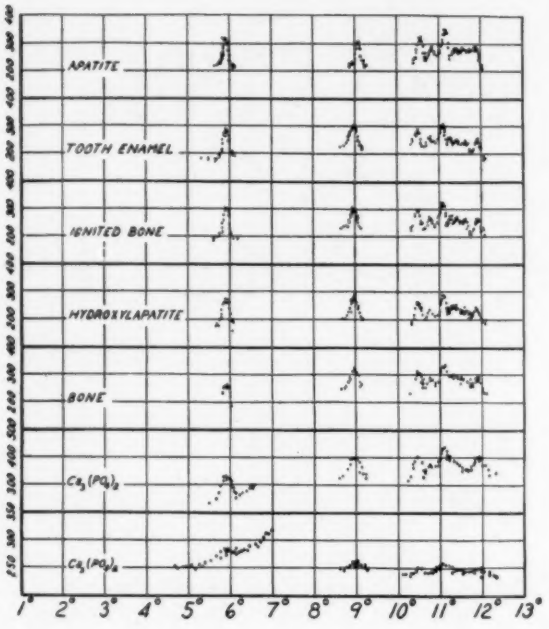

FIG. 3. Experimental powder diffraction data. The above data on apatite-like substances are plotted directly as recorded from a powder diffraction spectrometer utilizing a Geiger-Müller counter for intensity measurements. The ordinate is in terms of counts per minute, abscissa in terms of θ. Each point represents the average counts per minute of a five minute run of the counter apparatus. The physical set-up of slit widths, dimensions of diffracting sample, etc, was the same for each of those five experiments.

The first $Ca_3(PO_4)_2$ curve is typical of most commercial tricalcium phosphate. The last curve indicates the extreme imperfection of the crystal structure of certain preparations with the calcium-phosphorus ratio of tricalcium phosphate.

stances. Due to the good resolving powers of the apparatus the relative widths of the diffraction maxima of apatite, enamel and hydroxylapatite can be compared with those of heat labile $Ca_3(PO_4)_2$, dentine and bone. It is believed that these experiments demonstrate conclusively that within very close limits the unit cell dimensions of enamel, dentine, bone, tricalcium phosphate hydrate, hydroxylapatite and ignited bone are the same.

Using the ionization spectrometer, structure factor measurements were made on a good fluorapatite crystal on the 002 to the 008 planes and also on the 100 to the 700 planes. These values are recorded in Table III. It may be noted that they are in good agreement with the published values of St. Náray-Szabó. Absolute intensity measurements leading to absolute F-value determinations were also made on the 002 and 130, 310 powder diffraction maxima of fluorapatite and tooth enamel. These values are included in Table III.

DISCUSSION OF EXPERIMENTAL FINDINGS

Roentgen-ray diffraction data on bone and teeth are confined entirely to powder measurements since single large crystals of these substances do not occur. Since fluorapatite can be obtained in large crystals and is thus more easily susceptible to roentgen-ray analysis, a logical approach to the problem of determining the structure of the bone and tooth unit cell is to determine what changes from the structure of fluorapatite are required for this substance to produce the diffraction pattern of bone and tooth substance. Also it should be possible to calculate whether any proposed structures for bone substance are inconsistent with this similarity of diffraction patterns.

It is necessary to know how closely the accepted structure of apatite will account for the experimental apatite diffraction pattern. Apatite belongs to space group C_{6h}^2, the contents of the unit cell being $Ca_{10}F_2(PO_4)_2$. Determinations of its structure have been published by Mehmel[4] and by St. Náray-Szabó.[3] Mehmel's structure determination, once the space group had been established, is based entirely upon packing and symmetry considerations. The structure given by St. Náray-Szabó is summarized in Table II. The roentgen-ray spectrometer was used by the latter to give absolute intensity measurements on the 001, 110, and 100 crystal faces. Calculated structure factors were also correlated with visual intensity estimates from a powder photograph of apatite. He describes the agreement as good. Mehmel's proposed structure is similar to that

of St. Náray-Szabó except that Mehmel placed the two fluorine ions at the $00\,0, 00\,\frac{1}{2}$ positions of the unit cell, rather than at the $00\,\frac{1}{4}, 00\,\frac{3}{4}$ positions.

In the case of a few isolated diffraction maxima, it is possible to obtain experimental F-values directly from powder diffraction data to compare with the values calculated from St. Nàray-Szabó's proposed structure. I, the intensity of a powder diffraction maxima, may be measured as the increased area under the diffraction maxima as compared with the adjacent background on intensity-diffraction angle graphs. I is usually considered to have the value:

$$I = K\mathcal{J}\frac{\mathrm{Cos}^2\,2\theta}{\mathrm{Sin}^2\theta\,\mathrm{Cos}^2\theta}F^2.*$$

K is a constant that may be evaluated either experimentally or from a knowledge of the physical constants of the apparatus. To obtain the results reported here, NaCl or SiO_2, substances with known structure factors, were mixed with the substance being studied to permit measurements of diffraction maxima in terms of the transmitted beam. In Table III are listed experimental values for several diffraction maxima of apatite and tooth enamel.

In general, however, it is not possible to obtain individual F-values from the experimental powder diffraction spectra of apatite. This is because the powder diffraction maxima are often so close together that

* For the source and justification of this expression see Wyckoff, R. W. G.: "The Structure of Crystals." Second Edition (1931). The Chemical Catalogue Co., New York, or Bragg and West.[19]

TABLE II

THE STRUCTURE OF APATITE

Atomic positions

1 F (a) $00\frac{1}{4}, 00\frac{3}{4}$.
4 Ca_I (f) $\frac{1}{3}, \frac{2}{3}, u;\ \frac{2}{3}, \frac{1}{3}, \bar{u}, \frac{1}{3}, \frac{2}{3}, \frac{1}{2}-u;\ \frac{2}{3}, \frac{1}{3}, u+\frac{1}{2}$.
6 Ca_{II}, 6 P, 6 O_I, 6 O_{II}(h), $uv\frac{1}{4};\ \bar{u}\bar{v}\frac{3}{4};\ \bar{u}, u-v, \frac{1}{4};$ $v-u, \bar{u}, \frac{3}{4};\ v, v-u, \frac{3}{4};\ u-v, , \frac{3}{4}$.
12 O_{III} (i) $xyz;\ \bar{x}\bar{y}\bar{z};\ x-y, x, z;\ \bar{y}, x-y, z;\ x, y,$ $\frac{1}{2}-Z;\ \bar{x}, \bar{y}, \frac{1}{2}+z;\ x-y;\ x, \frac{1}{2}+z;\ \bar{y}, x-y, \frac{1}{2}-z;$ $y, y-x, \frac{1}{2}+z;\ y-x, \bar{x}, z;\ y, y-x, \bar{z};\ y-x, x,$ $\frac{1}{2}-z$.

Parameter Values, according to St. Náray-Szabó.[3]

	x/a	y/a	z/c
2 F	0	0	0.250
4 Ca_I	0.333	0.333	0
6 Ca_{II}	0.250	0	0.250
6 P	0.416	0.361	0.250
6 O_I	0.333	0.500	0.250
6 O_{III}	0.600	0.467	0.250
12 O_{III}	0.333	0.250	0.062
Suggested new 6 Ca_{II} Parameters			
6 Ca_{II}	0.237	−0.015	0.250

TABLE III

EXPERIMENTAL DIFFRACTION DATA APATITE (MoKα = .710 Å)

Indices	sin θ	F (exp) St. Náray-Szabó	F exp. (Bale) single crystal	F exp. powder	F exp. tooth enamel
002	0.1035	−135	117	108	112
004	.2070	188	202		
006	.3105	85	70		
008	.4104	99	90		
100	.0436	0	15		
200	.0872	24	28		
300	.1308	132	110		
400	.1744	18	18		
500	.2180	17	12		
600	.2616	23	18		
700	.3052	19	18		
130, 310	.1579			98	102

they cannot be independently resolved and because planes with indices of the type ABC and BAC have different F-values but coincident diffraction maxima.

The method adopted for comparing calculated F-values with intensities of the experimental spectra in such cases was to calculate by the aid of expression[1] the diffraction spectra predicted by these calculated F values, and to compare it with the experimental curve. Figure 1, *e*, represents graphically intensities *I*, which are calculated using St. Náray-Szabó's calculated F-values, and his values for the Bragg angle recalculated for Mo Kα radiation. This chart may be considered to be the powder diffraction pattern predicted by St. Náray-Szabó for apatite and therefore may be compared with the experimental curve 1, *b*. A similarity in the line intensities and positions of the experimental and constructed diffraction patterns is apparent. There may also be noted at various points quite wide variations between the two diagrams. The predicted diagram varies more widely from the experimental apatite curve than the experimental curve of tooth enamel does. Therefore the diagram constructed from St. Náray-Szabó's F-values cannot be of any great value in determining the difference in structure between tooth enamel and apatite.

As a first step toward a better understanding of the powder diagram of apatite, a recalculation of F-values from St. Náray-Szabó's apatite structure was undertaken. This was to detect, if possible, any errors that might be embodied in his F-values. It should be noted that errors that would be unimportant in his structure determinations become important in differential studies of substances with fundamentally similar structures. Experimental F-values as functions of θ for O^{2-} and P^{5+} have been computed by West[20] from the results of his structural determination of KH_2PO_4. Experimental Ca^{2+} values are given by Bragg and West.[19] These are probably the values used by St. Náray-Szabó in his F calculations. The source of his F values for fluorine is not known. F values for F^- given by Wyckoff and Armstrong[21] have been used for the calculations reported here. All of these F values are in general quite similar to values given by other observers for these ions, which is perhaps an indication of at least an approximate correctness.

Structure factor values up to angles including the 004 diffraction maxima were calculated. The results are tabulated in Table IV. Figure 1, *d*, represents calculated diffraction patterns computed from these values in the same manner as Figure 1, *e*. It will be noted (Fig. 1, *d*) that the agreement is considerably better between this calculated diffraction pattern and the experimental one than in the preceding case. This is evidence that the structure as determined by St. Náray-Szabó is essentially correct.

The agreement between predicted and experimental powder diffraction spectra is still not as good as it was hoped to obtain. Referring to Tables III and IV the calculated F-value for 130, i.e. +82.2, is considerably smaller than the experimental value of 98. The F-value of 310 is small and it would take considerable structural variation to make its contribution to this diffraction maxima of any significance. For 130 the oxygen contributions are calculated as 82 of a possible 96. This value cannot be greatly increased by a change in oxygen parameters. Shifts of the phosphorus parameters in various directions indicate that any likely P position cannot greatly increase the F-value of the cell. The F-value of fluorine is the same in either the 000 or 00$\frac{1}{4}$ positions, 11.8. Thus only a shift in the parameters of the 6 Ca ions appears likely to increase the F-value of the 310 maxima sufficiently. Tests show that a shift in these parameters from the .250,.000,.250 positions of St. Náray-Szabó to .237, −.015, .250 substantially improves the agreement between calculation and experiment. Other calculations show that there is an improved correspondence at other points in the diffraction pattern

TABLE IV

CALCULATED DIFFRACTION DATA FOR APATITE (Mo $K\alpha = .710$ Å)

Indices (Miller)	Apatite θ	Tooth enamel θ	Apatite			
			F calc. by St. Náray-Szabó	F calc. from St. Náray-Szabó Structure	F calc. with new Ca positions	Number of planes
100	2° 33′	2° 28′	− 12	− 13	− 11	6
101	3° 52′	3° 51′			5	12
110	4° 21′	4° 18′	7	4	6	12
200	5° 1′	4° 58′	− 42	− 40	− 34	6
111	5° 16′	5° 14′	− 30	− 12	− 9	12
201	5° 49′	5° 47′	17	19	8	12
002	5° 55′	5° 55′	−124	−115	−109	2
102	6° 26′	6° 26′	− 12	− 43	− 38	12
120	6° 38′	6° 34′	− 23	− 18	− 14	6
210	6° 38′	6° 34′	− 57	− 63	− 60	6
121	7° 17′	7° 13′	− 62	− 62	− 57	12
211	7° 17′	7° 13′	− 92	− 82	− 93	12
112	7° 21′	7° 20′	87	66	70	12
300	7° 32′	7° 28′	121	118	112	6
202	7° 47′	7° 44′	− 30	− 48	− 44	12
301	8° 6′	8° 2′	39	24	15	12
220	8° 43′	8° 37′	− 20	7	2	6
122	8° 55′	8° 52′	32	6	9	12
212	8° 55′	8° 52′	− 32	− 30	− 18	12
130	9° 4′	8° 59′	118	74	95	6
310	9° 4′	8° 59′	− 2	− 18	− 35	6
221	9° 13′	9° 7′	− 22	− 7	− 18	12
103	9° 15′	9° 15′	− 28	4	7	12
131	9° 34′	9° 28′	24	23	19	12
311	9° 34′	9° 28′	0	− 24	− 26	12
302	9° 37′	9° 33′	28	24	34	12
113	9° 56′	9° 54′	25	44	41	12
400	10° 5′	9° 58′	− 32	43	40	6
203	10° 15′	10° 13′	30	19	28	12
401	10° 31′	10° 25′	12	13	13	12
222	10° 34′	10° 29′	108	91	96	12
132	10° 52′	10° 47′	− 43	− 54	− 60	12
312	10° 52′	10° 47′	− 52	− 60	− 38	12
230	10° 59′	10° 53′	− 64	− 62	− 47	6
320	10° 59′	10° 53′	0	− 8	− 15	6
123	11° 10′	11° 6′	42	53	50	12
213	11° 10′	11° 6′	60	82	88	12
231	11° 24′	11° 17′	45	52	41	12
321	11° 24′	11° 17′	38	43	48	12
140	11° 34′	11° 26′	71	77	83	6
410	11° 34′	11° 26′	75	79	66	6
303	11° 42′	11° 39′	− 19	− 15	− 21	12
402	11° 43′	11° 39′	− 70	− 90	74	12
004	11° 55′	11° 55′	204	187	187	2
411	11° 57′	11° 50′	− 9		21	12
141	11° 57′	11° 50′	31		− 5	12

produced by this small parameter shift.

Further small shifts of Ca, P, and O parameters in various likely directions gave no appreciable improvement in the agreement of predicted and experimental diffraction diagrams. These shifts tested were by no means all of the possible ones, the tests being limited by the excessive amount of time required for such calculations.

A shift in the fluorine positions from the values of St. Náray-Szabó to the 000, $00\frac{1}{4}$ positions possible improves the correspondence of the 222, 132 and the 402 diffraction values, experimental and calculated, but produces a definitely poorer agreement in the case of the 102, 200, and 112 planes. Most of the other intensity maxima are not affected by this shift. It is likely that there is a greater heat motion in the Z-direction for fluorine than has been assumed in the F-values assigned to fluorine for the previous calculations. As a possible corrective for this greater heat motion, it was assumed that the Z-parameters are thus indeterminate and 000, $00\frac{1}{2}$ positions were given one-third the weight of the $00\frac{1}{4}$, $00\frac{3}{4}$ positions in structure factor calculations. Table IV gives the new F-values calculated assuming the new Ca positions and with the F-values for fluorine as described above. The calculated diffraction diagram shown in Figure 1, *c*, is obtained.* The agreement between calculated value and experiment can be described as good. No serious disagreement is produced between St. Náray-Szabó's experimental F-values and F-values calculated on this assumption of this shift of the Ca parameters of the indeterminacy in the position of fluorine.

In Figure 2, *c*, has been plotted the calculated diffraction spectrum of apatite, using the data from which Figure 1, *c*, was plotted with the exception that the θ's calculated from the experimentally measured unit cell of enamel and listed in Table IV have been utilized. It may be noted that the agreement between this curve and the experimental diffraction pattern for enamel directly above is good, in fact much better than the agreement between the experimental curve for enamel and the calculated apatite curve (Fig. 1, *c*). Therefore, the principal cause of the differences between the diffraction pattern of apatite and that of enamel, at least to diffraction angles as great as that corresponding to the 004 diffraction maxima, is the small but definite variation in unit cell dimensions.

Since the diffraction pattern of hydroxylapatite appears indistinguishable from tooth enamel, its structure must also be very close to that of fluorapatite. Probably the essential difference is the substitution for fluorine ions of the similarly sized hydroxyl ions.

Trömel and Möller,[22] and Hodge, LeFevre, and Bale[7] have presented evidence from chemical studies that the so-called tricalcium phosphate hydrates are essentially hydroxylapatites with additional phosphorus present in what has been described as an absorbed state on the small hydroxylapatite crystals. The roentgen-ray diffraction measurements reported in this paper show increased width of the diffraction maxima of tricalcium phosphate as compared with hydroxylapatite but the same unit cell dimensions. This result, which is interpreted as indicating either the extremely small size of the crystals making up the tricalcium phosphate hydrate, or the great imperfection of these crystals, or both, is consistent with the interpretation given above based on chemical data.

Considerable amounts of carbon exist in bone and tooth substance, approximately sufficient to allow one CO_3^{2-} per unit cell, although carbon is the most variable of the major constituents of teeth and bone. Since carbonates have never been identi-

* In a private communication, Bredig has called attention to the difference in the number of theoretical and experimental maxima in Figure 1, especially in the region between diffraction angles 11 and 12 degrees. He suggests that such variations might arise from various proportions of CO_3 to F in a mixed apatite. It seems more likely, however, that this variation is due to random fluctuations in the experimental data, i.e., experimental errors, since other measurements show the theoretical number of maxima in this region.

fied in diffraction patterns of these substances as separate crystalline constituents, it is tempting to suppose that the carbonate forms an integral part of the crystal lattice of tooth and bone, and that these substances are therefore basically carbonate-apatites. There are two possible positions for the carbonate radical in the apatite structure. Hendricks, Hill, Jacobs and Jefferson[23] suggest that the CO_3^{2-} radical occupies the position of one of the F^- ions of the unit cell, the empty position of the other fluorine ion being occupied by an uncharged water molecule. Hendricks, Jefferson and Mosley[5] later suggested that the water molecule and the carbonate radical are in the 000, and $00\frac{1}{2}$ positions. Since the diffraction patterns of tooth and bone substance and of hydroxylapatite are so very similar it seems pertinent to inquire how much distortion of the apatite lattice would be produced by such substitutions. Several investigators have stated that there is not room in the apatite lattice for the carbonate radical. However, no quantitative data on this question have so far been published.

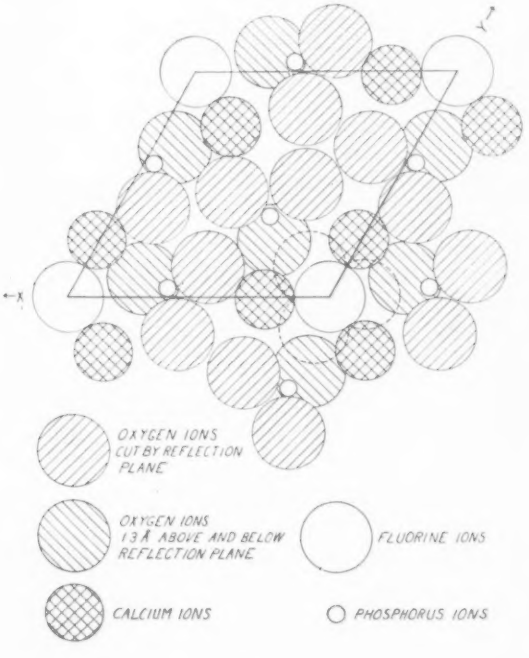
OXYGEN IONS CUT BY REFLECTION PLANE
OXYGEN IONS 1.3 Å ABOVE AND BELOW REFLECTION PLANE
FLUORINE IONS
CALCIUM IONS
PHOSPHORUS IONS

Fig. 4

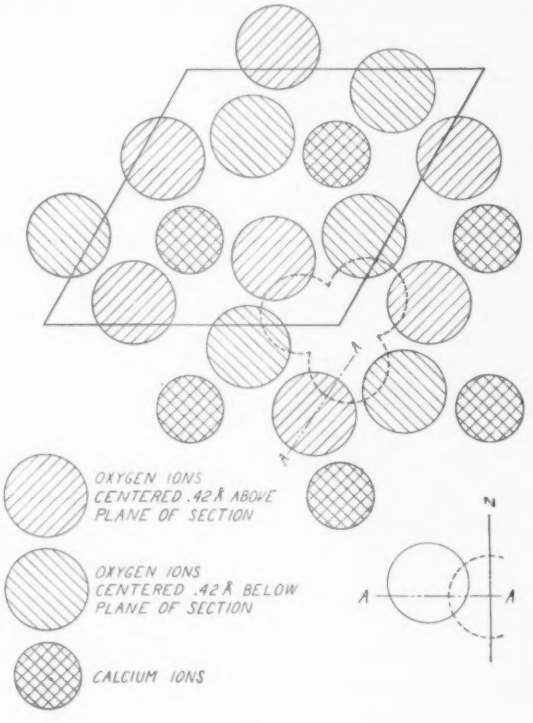

Fig. 5

Numerous investigators have studied the nature of the CO_3^{2-} radical in several compounds, calcite perhaps most elaborately. In such compounds, without exception, the carbonate radical has been found to be strictly planar with the central carbon 1.26 Å from the centers of the surrounding O^{2-} ions which are placed at the corners of an equilateral triangle 2.18 Å on a side. Between metallic ions (for instance, the calcium ions of calcite) and oxygen centers, the distance is that indicated by the usual O^{2-} radius of 1.26 Å.

Figure 4 represents a section of the fluorapatite structure at the $z = \frac{1}{4}$ level. The dotted figure indicates the space that the carbonate radical would occupy if it replaced fluorine at $00\frac{1}{4}$. Figure 5 is a section of the apatite structure at the $z = 0$ level with the carbonate radical indicated in the 000 position. Even with considerable allowance for the slightly increased size of the hydroxylapatite lattice and for variations in packing size it seems quite unlikely that a carbonate apatite would be

formed without marked variation in atomic parameters as compared with a hydroxylapatite containing no carbonate. Calculations show that even small variations in atomic parameters should produce noticeable variations in the diffraction pattern. It is therefore unlikely that the diffraction pattern of bone substance is principally that of a carbonate apatite, although occasional replacements of this type may exist.

Gruner, McConnell and Armstrong[24] suggest that carbon may replace calcium and also phosphorus in the apatite structure of bone and tooth substance, giving in the case of phosphorus replacement a CO_4 grouping. The data presented here can neither affirm nor deny these hypotheses. However, this structure seems unlikely since carbon is not known otherwise to form this type of structure.

It is probable that the portion of tooth and bone substance responsible for its characteristic diffraction pattern is essentially hydroxylapatite. That variations and distortions of this apatite structure are common in tooth and bone substance is indicated by the increased breadth of the diffraction maxima of these substances as compared with fluorapatite. It is in such structural discontinuities that the excess phosphate of tricalcium phosphate hydrate is probably found. Since the diffraction patterns of tooth and bone substance give no indication of appreciable amounts of a carbonate apatite being present, the carbonate ions are also, probably, most abundant in these regions of structural discontinuity that may be considered as marking the transition from one crystalline particle to another. Thus the carbonate contribution is mainly to the random element responsible for the diffuseness of the hydroxylapatite diffraction pattern of tooth and bone rather than toward producing a characteristic carbonate apatite diffraction spectrum of its own.

I wish to thank Dr. Stafford L. Warren, Dr. Harold C. Hodge, Miss Marian LeFevre, and Mr. Francis Bishop for assistance in various phases of this work. This work was supported in part by a grant from the Rockefeller Foundation.

SUMMARY AND CONCLUSIONS

1. Powder diffraction data reported here indicate that the structure proposed by St. Náray-Szabó for fluorapatite must be nearly correct. Slight shifts in the apatite parameters are found, which give appreciably better agreement between calculated diffraction intensities and the diffraction data reported. Parameters of these structures are given in Table II.

2. The dimensions of the unit cells of bone, tooth enamel, dentine, hydroxylapatite and tricalcium phosphate hydrate are measured and are found to be identical within the range of experimental error. They give closely similar apatite-like patterns which, in minor points mainly due to a difference in the a-dimension of the unit cell, are significantly different from fluorapatite.

3. That portion of bone and tooth substance responsible for its characteristic diffraction pattern tends to approximate the structure of hydroxylapatite. It is concluded, however, that present roentgen-ray diffraction evidence is consistent with a considerable lack of homogeneity in the nature of tooth and bone substance.

4. Probably the carbonate present in tooth and bone substance does not form an integral part of the apatite lattice, but is rather present, for the most part at least, at boundary and transition regions in the lattice where the apatite structure is imperfectly developed.

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EDITORIAL

INTRACRANIAL COLLECTIONS OF IODIZED OIL FOLLOWING LUMBER MYELOGRAPHY

DANDY, in 1919, was the first to use air in the spinal canal as a contrast medium for the localization of spinal cord lesions. Following quickly upon the heels of Dandy's observation, Sicard and Forestier introduced lipiodol into the spinal canal and this contrast medium has been of valuable aid in the diagnosis and localization of certain lesions of the spinal cord. This, however, has one disadvantage in that it has been known for a long time that the opaque oil remains indefinitely in the spinal canal unless it is removed at operation, which is usually very difficult and seldom can be accomplished as the oil often is scattered throughout the cerebrospinal fluid pathway. It has been believed for some time that the oil is somewhat irritating and that it may be encapsulated in or about the lower portions of the spinal sac. For this reason warnings have been issued against the indiscriminate use of opaque oil within the spinal canal.

Chamberlain and his coworkers have shown that with modern technique air may be useful as a contrast medium; particularly is this true in thin subjects, and Chamberlain has been the great exponent in advocating the use of air instead of opaque oils. However, in the hands of most observers the oil has furnished far more conclusive results than have the air myelographic studies.

Quite recently Garland and Morrissey* became interested in the question of intracranial collections of iodized oil following myelography. A survey of the literature revealed no specific information on clinical symptoms or pathologic changes due to prolonged retention of lipiodol intracranially, although there was considerable material on late changes in and about the meninges of the cord. In order to throw a little more light on the problem and to study it under clinical conditions, they decided to have return for examination a group of patients who had had lipiodol injected into their spinal canal several years previously, and they have quite recently reported their observations.

It has been known for some time that there are certain reactions to the subarachnoid injections of iodized oil and also that mild reactions follow the injection of air. These reactions may be immediate as shown in the elevation of the spinal fluid cell count and slight hyperemia about the site of injection, and clinically there may be slight headache, increase in the pain of which the patient is complaining, slight fever, and sometimes pain about the sacrum and coccyx. These symptoms and clinical signs usually subside in from two to five days. Occasionally late reactions are manifested in coccygeal pain which usually subsides within three months. The oil may lie in small droplets and lakes scattered up and down the spinal canal, sometimes extending out along the nerve sheaths. Occasionally the oil may be encapsulated in the cul-de-sac at the base of the spinal canal. After about three years these droplets tend to become encapsulated in various areas and fibroblastic proliferation and pseudogranulomas may develop about the oil.

It is these late manifestations which have prompted neurosurgeons to attempt to remove some if not all of the oil at the time of laminectomy, but this is a rather

* Garland, L. H., and Morrissey, E. J. Intracranial collections of iodized oil following lumbar myelography. *Surg., Gynec. & Obst.*, Feb. 1, 1940, *70*, 196–210.

difficult procedure and is not always accomplished, and it has been suggested by some that undue efforts at removal of the oil may do more harm than leaving the oil *in situ*.

Garland and Morrissey, in a review of their cases showing lipiodol in the cranial cavity, have attempted to clear up some of the clinical impressions regarding the presence of lipiodol or other opaque oil in the cranial cavity, since the previous reports on this have been somewhat vague.

The patients which they restudied had had subarachnoid lipiodol injections from one to thirteen years previously, 3 to 5 cc. of the oil having been used in most instances.

In the study their attention was called to the fact that iodized oil may be found scattered throughout the subarachnoid space over the cerebrum and cerebellum, in the basal cisternae, and even in the ventricles years after its injection into the lumbosacral sac. Approximately two-thirds of their cases showed collections of varying amounts of lipiodol intracranially but none of these patients except one exhibited any symptoms which were not present before the lipiodol injection was made. The one case that was somewhat at variance with these observations was a patient who proved later to be a malingerer. Garland and Morrissey call attention to the danger of drawing premature conclusions from the finding of iodized oil in the leptomeninges of the brain and spinal cord. In their group of cases it was noted that the intracranial lipiodol tends to become fixed, that is, immovable, whereas iodized oil in the spinal canal, especially when in large collections, is sometimes freely movable even up to a period of fourteen years following injection. They were unable to explain why in only two-thirds of their cases iodized oil was found intracranially following the intraspinal injection. In order to determine this point they are inquiring into the patients' occupation or postural habits, whether the group that showed intracranial lipiodol were employed in work which involved frequent lowering of the head.

From a critical analysis of their cases they came to the conclusion that there were no symptoms or positive neurological findings which could be ascribed to the presence of the oil intracranially.

While it is of the greatest importance to learn that the presence of lipiodol in the intracranial cavity is not in itself productive of symptoms, the *indiscriminate* use of lipiodol in the study of suspected spinal cord lesions is to be deplored, and only in those carefully selected cases is one justified in using it as a diagnostic procedure.

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Items for this section solicited promptly after the events to which they refer.

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SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
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RADIOLOGICAL SOCIETY OF NORTH AMERICA
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RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
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RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
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SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
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RADIOLOGICAL SECTION, LOS ANGELES CO. MED. SOC.
Secretary, Dr. Wilbur Bailey, 2007 Wilshire Blvd., Los Angeles, Calif. Meets on second Wednesday of each month at County Society Building.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. L. J. Taormina, 1093 Gates Ave., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. C. J. Challenger, 3117 Logan Blvd. Meets second Thursday of each month October to May inclusive at the Hotel Sherman.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. H. A. Mahrer, 10515 Carnegie Ave. Meets at 6:30 P.M. at Mid-Day Club rooms on fourth Monday each month, October to April, inclusive.

DENVER RADIOLOGICAL CLUB
Secretary, Dr. P. R. Weeks, 520 Republic Bldg., Denver, Colo. Meets third Friday of each month.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

FLORIDA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. J. N. Moore, 210 Professional Bldg., Ocala, Florida. Meetings in May and November.

GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meetings held quarterly, on the fourth Sunday of the month.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. C. C. Taylor, 23 E. Ohio St., Indianapolis, Ind. Meeting held the second Sunday in May annually.

KENTUCKY RADIOLOGICAL SOCIETY
Secretary, Dr. J. C. Bell, 402 Heyburn Bldg., Louisville. Meets annually in Louisville on third Sunday afternoon in April.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. J. E. Lofstrom, 1536 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. I. I. Cowan, Mt. Sinai Hospital, Milwaukee, Wis. Meets monthly on first Friday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. J. P. Medelman, 572 Lowry Medical Arts Bldg., St. Paul.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M., at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. A. O. Hampton, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. W. J. Marquis, 198 Clinton Ave., Newark. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. R. D. Duckworth, 170 Maple Ave., White Plains, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year—January, May, November.

PACIFIC ROENTGEN CLUB
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport, Pa. Next annual meeting, Hershey Hotel, Hershey, Pa., May 17–18, 1940.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. H. W. Jacox, 4800 Friendship Ave., Meetings held second Wednesday each month, 4:30 P.M., October to June at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. S. C. Davidson, 277 Alexander St. Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

SAN FRANCISCO RADIOLOGICAL SOCIETY
Secretary, Dr. H. A. Hill: 450 Sutter St., San Francisco. Meets monthly on third Thursday at 7:45 P.M., first six mouths at Toland Hall, second six months at Lane Hall.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

South Carolina X-Ray Society
Secretary, Dr. Hillyer Rudisill, Jr., Roper Hospital, Charleston. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg. Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. L. W. Baird, Scott and White Hospital, Temple, Texas. Next annual meeting, January 18, 1941, Sherman, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. V. W. Archer, University Hospital, University, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. K. J. Holtz, American Bank Bldg., Seattle. Meets fourth Monday of each month at the College Club, Seattle.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets monthly on third Thursday, from November to June inclusive, at 8:15 P.M., 32 Welbeck St., London.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

Faculty of Radiologists
Secretary, Dr. Barbara M. Key, 32 Welbeck St., London, W. 1, England.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive for scientific discussion.

Canadian Association of Radiologists
Secretary, Dr. A. C. Singleton, Medical Arts Bldg., Toronto, 5, Ontario.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N.S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium). Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel. Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent Secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the spring, and one in the fall.

Societa Italiana Radiologia Medica
Secretary, M. Ponzio, University of Turin, Prof. Turin

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly on first Monday at 8 o'clock.

Polish Society of Radiology
Secretary, Dr. Jan Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St. Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime:

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen. Meets the second Wednesday of each month from October to July in Copenhagen, at 8 'oclock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6:30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University. Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto, Japan. Meets bi-monthly on third Sunday.

AMERICAN ROENTGEN RAY SOCIETY

SECTION ON INSTRUCTION

B. R. Kirklin, M.D., *Director*

Abstracts of Courses Offered

Forty-first Annual Meeting

Hotel Statler, Boston, Massachusetts

October 1–4, 1940

President-elect Sosman, with the approval of the Executive Council, has directed that the Section on Instruction be continued for the 1940 annual meeting. He has arranged his program so that the instruction courses will be given between the hours of 2:00 P.M. and 4:30 P.M. on Tuesday and Thursday, and 2:00 P.M. and 5:45 P.M. on Wednesday and Friday. Nothing else will be scheduled during these hours, thus allowing everyone at the meeting to attend two or three instruction courses each afternoon.

This Section presents for 1940:

1. Four single-period Special Clinical Lectures.
2. One three-period Sequential Course.
3. Two single-period courses on Miscellaneous Subjects.
4. Thirty-six single-period courses on Diagnostic Roentgenology, with a faculty of forty instructors and covering forty-two periods.
5. Twenty-five single-period courses on Therapeutic Radiology, with a faculty of twenty-six instructors and covering thirty-one periods.

GENERAL INFORMATION

Conference Periods

Tuesday, Wednesday, Thursday and Friday afternoons

First period	2:00 to 2:50
Second period	3:00 to 4:15

Wednesday and Friday afternoons

Third period	4:30 to 5:45

Location

One of the single-period Special Lectures, lettered "SL-1" to "SL-4" will be given during the first period (2:00 to 2:50 P.M.) each day. Due to the anticipated popularity of these Special Lectures no other courses will be scheduled for the first period on any day and they will be given in the Georgian Room on the Mezzanine Floor. *All other courses given during the second and third periods will be given on the fourth floor.*

The instruction periods will be designated with the following code:

T-1	Tuesday, first period	2:00 to 2:50
T-2	Tuesday, second period	3:00 to 4:15
W-1	Wednesday, first period	2:00 to 2:50
W-2	Wednesday, second period	3:00 to 4:15
W-3	Wednesday, third period	4:30 to 5:45
Th-1	Thursday, first period	2:00 to 2:50
Th-2	Thursday, second period	3:00 to 4:15
F-1	Friday, first period	2:00 to 2:50
F-2	Friday, second period	3:00 to 4:15
F-3	Friday, third period	4:30 to 5:45

(Familiarity with this code will avoid much confusion)

How to Secure Tickets for Instruction Courses

Admission to the Instruction Courses will be by ticket only.

Following the abstracts of the courses will be found a pink general order sheet. First, second and third choices for the second and third periods should be carefully selected as the number attending each course given during these periods will be limited to from thirty to fifty persons. It is not necessary to indicate second and third choices for the first period as only

one of the Special Clinical Lectures will be given during the first period each day. If directions as given on the order sheet are followed explicitly, errors in completing reservations will be minimized.

It is possible for one to attend only ten periods of instruction so the condensed schedule should be noted carefully in arranging individual orders for tickets.

Reservations will be made in the order of receipt of the pink forms. Those who are not members of the American Roentgen Ray Society will be charged a nominal fee of $1.00 per period, or a maximum fee of $5.00 for five or more periods. Full time graduate students in Radiology will be admitted without fee.

If the courses are not filled by the time of the meeting, tickets will be available at the registration desk, located on the Mezzanine Floor, on Sunday, September 29, and thereafter during the meeting.

Holders of Tickets

Those who do not have a proper ticket for the assigned course will not be permitted to enter the room. Pages will be assigned to each conference room to collect tickets.

Duplications and Repeats

Due to the anticipated heavy registration a few courses will be repeated and others will be duplicated by two or more instructors.

SPECIAL CLINICAL LECTURES

COURSE: SL-1

Georgian Room **Period: T-1**

SHIELDS WARREN, M.D., Boston, Mass.

The Radiosensitivity of Tumors

The varied response of different types of tumors to radiation still rests on an empirical basis, although in general the less differentiated tumors respond better than highly differentiated ones. The response hinges not only on the character of the tumor itself, but also on the character of the supporting tissue, the presence or absence of associated infection, and whether or not previous radiation has been given.

Tumors may be grouped into three classes: radiosensitive, which regress with dosages that do no permanent damage to adjacent normal tissue; radioresponsive, that regress with doses producing moderate damage to normal tissue; and radioresistant, that fail to regress or do so only with dosages that do serious injury to normal tissues.

In the response to radiation, the direct effect on the type cell of the tumor, the alteration of the connective tissue of the stroma, and the injury to stromal blood vessels all play important parts.

The factors that bring about increased radioresistance of tumors following their initial irradiation are not clearly defined, but undoubtedly stromal and vascular changes play an important part.

Examples of various types of sensitive and resistant tumors will be shown.

COURSE: SL-2

Georgian Room **Period: W-1**

GERRY B. SCHNELLE, V.M.D., Boston, Mass.

Roentgen Rays in Veterinary Medicine

This will be an "Information Please" type of program with the lecturer presenting roentgenograms of animals, showing the unusually varied diseases and tumors that animals are subject to. Most of these conditions can be readily diagnosed by their similarity to the roentgen findings in man.

There will be three "experts" who will take turns in attempting to make the diagnosis from the roentgenogram.

Lantern slides will be used for the audience.

COURSE: SL-3

Georgian Room **Period: Th-1**

W. B. CASTLE, M.D., Boston, Mass.

Leukemia

A comprehensive clinical discussion of leukemia will be presented including the differential diagnosis, prognosis, treatment and care of patients from the non-radiological aspect.

COURSE: SL-4

Georgian Room **Period: F-1**

FULLER ALBRIGHT, M.D., Boston, Mass.

Osteoporosis

The term "osteoporosis" will first be defined. In order to do this a schematic chart will be presented

which will represent the calcium and phosphorus metabolism in the normal individual. Schematic charts will then be presented of various generalized metabolic disorders. These will include osteomalacia, osteitis fibrosa, Paget's disease, and osteoporosis. The clinical conditions which lead to osteoporosis will then be discussed. One special entity which is termed post-menopausal osteoporosis will be emphasized. Some metabolic data showing the effects of hormonal therapy on post-menopausal osteoporosis will be presented. Certain cases will be discussed in which two metabolic bone diseases occurred in the same patient, e.g. osteoporosis and Paget's disease, osteoporosis and hyperparathyroidism.

SEQUENTIAL COURSE: A

Room: 400 **Periods: T-2; W-2; Th-2**

JOHN T. MURPHY, M.D., Toledo, Ohio

Malignant Bone Tumors

Both the roentgenologic and microscopic findings of malignant tumors of bone will be shown and discussed. The clinical course of the disease will be stressed and a complete follow-up of each patient will be presented. Considerable time will be devoted to the differential roentgenologic diagnosis.

This course will be conducted as a teaching seminar and all those in attendance may participate in the discussion.

This is a sequential course and no part of it will be repeated.

SINGLE PERIOD COURSES

MISCELLANEOUS

COURSE: 101

Room: 412 **Period: Th-2**

ARIAL W. GEORGE, M.D., Boston, Mass.

Roentgenology in Industrial Medicine and Automobile Accidents; The Roentgenologist as an Expert Witness

This course will consist of a discussion of:

1. The importance of careful and concise reports on industrial and accident cases.
2. The importance of exactness of diagnosis and proper use of medico-roentgenologic terms (nomenclature).
3. The rôle that industrial and accident roentgenology plays in medicolegal expert testimony.
4. Some of the pitfalls that experts, especially roentgenologists, are likely to encounter.
5. Some of the fundamentals of court procedure relative to the plaintiff as well as the medicolegal expert (roentgenologist) for the defense—the latter's rights under the law.
6. The controversial subject "Arthritis of the Vertebrae" and its importance in industrial roentgenology.

The instructor will be glad to have any of those attending the course bring controversial films with them.

COURSE: 102

Room: 413 **Period: W-3**

GEORGE C. HENNY, M.Sc., M.D., Philadelphia, Pa.

Roentgen Film Characteristics and the Practical Calibration of Roentgenographic Apparatus and Processing Solutions

The characteristics of the roentgen film emulsion (together with intensifying screens if they are used), in which the roentgenologist is mainly concerned, are the "speed" and the "contrast." These characteristics are of great importance.

The "speed" determines the degree of darkening of the processed film, after standard development, for a given roentgenographic exposure and a particular anatomic part.

The "contrast," under the same conditions, determines the degree to which tissue density-differences and thickness-differences of the anatomic part will be recorded on the roentgenogram.

For uniformity of results the roentgenographic apparatus and processing solutions should be calibrated at regular intervals. Fairly simple methods of calibration, which are accurate enough for the purpose, are described and may be employed in the roentgen department without great outlay of time or money. When properly employed the roentgenograms of a given patient show uniform density from one examination to the next and the detail of the anatomic parts being studied is, as far as the film emulsion is concerned, brought out to the greatest degree.

SINGLE PERIOD COURSES

DIAGNOSTIC ROENTGENOLOGY

COURSE: 201

Room: 402 **Period: F-3**

V. W. ARCHER, M.D., University, Va.

Roentgenologic Manifestations in Osteomyelitis

Negative findings early in the disease. Examples of atypical disease. Roentgenographic demonstration

of structural weakness necessitating immobilization to prevent deformity. Demonstration of sequestra and pockets as cause of draining sinuses. Brodie's abscess. Late recurrences. Differential diagnosis between osteomyelitis, lues, mycotic infection, tuberculosis, and tumor.

COURSE: 202

Room: 402 **Period: W-3**

VINCENT W. ARCHER, M.D., University, Va.
F. B. BOGART, M.D., Chattanooga, Tenn.

Chest Findings in "Country Diseases"

Pulmonary findings in (1) tularemia; (2) pneumonia; (3) pleural effusion; (4) bronchitis; (5) nodular infiltration; (6) actinomycosis; (7) blastomycosis; (8) Malta fever.

COURSE: 203

Room: 402 **Period: T-2**

PAUL A. BISHOP, M.D., Philadelphia, Pa.

Examination and Diagnosis of Lesions of the Temporomandibular Joint

The frequency with which injuries of the temporomandibular joint are overlooked, both clinically and roentgenographically, has led to an appalling number of permanent, serious disabilities of the mandible. A technique for the roentgenographic study of this joint is presented with lantern slide demonstration of acute and chronic injuries, as well as various non-traumatic conditions.

COURSE: 204

Room: 401 **Periods: Th-2; F-3**

RALPH S. BROMER, M.D., Philadelphia, Pa.

The Differential Diagnosis of Skeletal Changes Occurring in Diseases of Infants and Children

The time allotted will be spent in discussing the differential roentgen diagnosis of skeletal changes occurring in diseases of infancy and childhood. All such diseases cannot be included in the time available for the course. Case material will be chosen from the following list: congenital syphilis, rickets, infantile scurvy, tuberculosis, lead poisoning, the blood dyscrasias, xanthomatosis and allied conditions, osteogenesis imperfecta, achondroplasia, multiple enchondromata, multiple cartilaginous exostoses, metastases caused by neuroblastoma, osteochondritis and endocrine disturbances. Wherever possible the early roentgen changes will be emphasized. The question of differential diagnosis will be approached from the standpoint of the predisposition of the various diseases to affect certain bones or certain areas of individual bones. Thus in the case of the long bones, differential roentgen signs of the disease processes in the epiphysis, the diaphysis, the metaphysis, the periosteum, cortex, etc., will be given in detail.

COURSE: 205

Room: 409 **Period: W-2**

P. F. BUTLER, M.D., Boston, Mass.

Consideration of Fractures from a Medicolegal Standpoint

The opinion of a roentgenologist in court must be based upon roentgenologic data, knowledge of pathology, and of the end-results of injuries. Since the question of permanent deformity and disability plays such an important part in the medicolegal evaluation of a case, special attention will be given to prognosis and the question of permanent deformity. The changes in the type of injuries since the advent of the automobile era will be discussed. The significance of certain types of skull fractures and the healing of such fractures will be considered. Particular emphasis will be placed on fractures involving the epiphyses in children and an accurate method of measuring leg length will be described.

COURSE: 206

Room: 408 **Period: F-3**

JOHN R. CARTY, M.D., New York City

Soft Tissue Roentgenography

The pathological and anatomical basis of soft tissue roentgenography is briefly discussed, with particular reference to the newer concepts regarding fascial planes.

The essential points of the technical procedures are discussed and emphasis is placed on the necessity for an adequate understanding of the technical factors if success in this field is to be expected. Only practical aspects are to be considered, and a simple technical procedure is outlined which may be followed with the equipment found in the average roentgenographic office or department.

Following the discussion of technique the pathological conditions in the soft tissues which may be demonstrated roentgenographically are discussed and divided into appropriate groups, as follows:

Vascular Conditions: Soft tissue roentgenography is valuable in the study of arteriosclerosis and varicose veins. Information may be obtained as to whether or not the deep veins are involved. Occa-

sional valuable information may be obtained regarding arteriovenous aneurysms.

Soft Tissue Tumors: Information regarding the extent and character and whether or not the tumor is malignant may often be secured following roentgenographic examination. It is my opinion that no examination for bone tumor is complete without a soft tissue study also. Differential diagnosis between fibroid periosteal sarcoma and osteogenic sarcoma may sometimes be made. The presence of minute deposits of calcium caused by osteogenic elements in the soft tissues is the deciding factor. These calcium dots are usually entirely obliterated in roentgenograms made for bone detail. In hemangiomata distribution and location of the vessels supplying the tumor can often be ascertained. This may be of considerable value to the surgeon.

Muscle Conditions: Calcified hematomata are well shown in a soft tissue study. Occasionally a ruptured muscle may be demonstrated. Early atrophy at times may be demonstrated before there is actual reduction in size of the limb.

Infectious Conditions: Soft tissue roentgenography is invaluable in the diagnosis of gas gangrene, particularly for determining the extent of the disease. Soft tissue roentgenography is useful in the study of elephantiasis and may help in the differentiation of various types of edema. Soft tissue study of inflamed bursae is helpful, particularly where there is an absence of calcium-like material.

Soft tissue roentgenography of the larynx is briefly discussed, with special reference to carcinoma, edema and retropharyngeal abscesses.

In conclusion, the technique and scope of fasciagraphy is briefly discussed, and films shown which demonstrate its usefulness in certain selected conditions.

COURSE: 207

Room: 406 **Period: T-2**

JAMES T. CASE, M.D., Chicago, Ill.

The Roentgenologic Diagnosis of Carcinoma of the Colon

In the diagnosis of carcinoma of the colon the pathological and anatomical considerations vary according to the location of the tumor in the right or left half of the colon. In colonic polyposis the symptomatology, like the pathology, varies with the position of the tumor in the right or left colon. Special technique is a matter of utmost importance. Repetition of the examination is often necessary.

The technique of examination for and the roentgenologic manifestations of cancer of the colon will be discussed and illustrated.

COURSE: 208

Room: 402 **Period: F-2**

W. EDWARD CHAMBERLAIN, M.D., Philadelphia, Pa.

Technique and Interpretation of Oxygen Myelography

Oxygen has now been used successfully in hundreds of cases as the contrast medium for myelography. It has many advantages over other media but the roentgenographic requirements are very exacting.

Lumbar puncture vs. cisternal puncture for introduction of the oxygen; methods of increasing scope of lumbar puncture route; adaptation of ordinary conventional roentgenographic apparatus to this work; essential factors in technique; stereoscopy essential in lateral as well as dorsal projections; stereoscopic shift across long axis of spine; value of comparing lateral projections with spine in hyperflexion and hyperextension; value of "over-exposing" films; oblique projections of little value except in cervical and upper thoracic regions; suggestions for after-care of patients.

COURSE: 209

Room: 401 **Periods: T-2; W-2**

ARTHUR C. CHRISTIE, M.D., Washington, D. C.

The Diagnosis and Treatment of Bronchiectasis

History and Incidence.

Etiology and Pathogenesis.

Diagnosis.

Symptoms and signs. Necessity and means of early diagnosis. Iodized oils. Instillation of iodized oil by the passive method. Description of method. Illustrative slides to show different types of bronchiectasis and conditions which may require differential diagnosis.

Treatment.

Necessity for treating complicating inflammatory conditions. Medication. Postural drainage. Iodized oils. Bronchoscopic drainage.

Surgery: Applicability and limitations. Artificial pneumothorax. Phrenicectomy. Pneumectomy.

Roentgen therapy: Rational basis for such treatment. Detailed descriptions of application, dosage, etc. Results illustrated by report of cases.

The aim of this course is to give a complete view of the diagnosis and treatment of this exceedingly common disease in which the radiologist can play an important rôle in both fields.

COURSE: 210

Room: 400 **Period: F-2**

E. A. CODMAN, M.D., Boston, Mass.
C. W. BLACKETT, M.D., Boston, Mass.

The Shoulder

The course will be divided into four parts:

1. *Normal motion of the shoulder.* This portion will consist chiefly of a demonstration of the "pivotal paradox" and one must understand the explanation of this in order to appreciate the normal motion of the shoulder.
2. *Complete roentgen examination of the shoulder.* The authors will demonstrate the optimum position in which the shoulder should be exposed in order to detect any ordinary lesion of this region in which the roentgen ray helped make the diagnosis.
3. *Pathologic conditions demonstrable by roentgen ray.* This will consist chiefly of a listing of the pathologic conditions which may be demonstrable by roentgen ray. These will be amply illustrated by lantern slides and the more unusual conditions will be demonstrated.
4. *Round table discussion.* The authors hope that each person registering for this course will send to Dr. Blackett one question, as this will give them an idea of what is most desired and an attempt will be made to answer these questions during the round table discussion.

COURSE: 211

Room: 409 **Period: Th-2**

LEWIS GREGORY COLE, M.D.,
New York City

Pneumoconiosis

1. Rapid demonstration of roentgenograms from various sources in this country and Canada, presented regardless of the extent and character of the lesion, to show the necessity of classification.
2. Properly and improperly prepared autopsy specimens compared with roentgenograms.
3. Dust in the lungs as observed microscopically with the light and dark fields.
4. Phagocytes and their effect on adjacent anatomical structures:
   a. Black phagocytes—not destructive.
   b. White phagocytes—destructive if overloaded.
   c. Black and white phagocytes—not destructive.
5. Roentgenographic findings are caused by four types of pathology:
   a. Dust flects phagocyted in clumps or streaks.
   b. Collagen (not connective tissue) laid down in four patterns: whorls, lamina, gobs, and strands.
   c. Demonstration of cells and debris within the alveoli and air passages.
   d. Increased ventilation:
      (1) Localized air cysts.
      (2) General emphysema.
6. Pathological changes in the alveolar wall, evidenced by hypertrophy, proliferation and desquamation of the alveolar lining, causing dyspnea.
7. Vascular and intervascular changes in pulmonary capillaries and blood vessels, resulting in
   a. Avascular areas.
   b. Hypervascular areas.
8. Lymph follicles are not the home of the silicotic (?) nodule. It is more free of pathology than any other structure in the lung.
9. Four types of pneumoconiosis constitute different pathological entities and different compensation problems.
10. Philosophy: And so, what?
    The application of these findings to a solution of the pneumoconiotic (silicotic) problem.

COURSE: 212

Room: 401 **Period: W-3**

HOWARD P. DOUB, M.D., Detroit, Mich.

The Invertebral Disc

This discussion will be limited as much as possible to the disc itself, but owing to its intimate relationship to the vertebrae, it will be necessary to consider the spine to some extent.

We wish to present the anatomy of the disc and its vascular supply together with reference to defects in its development which often lead to abnormalities in later life. Changes in the fibrous structure and in the cartilage plates, due either to disease or trauma, will be brought out. The effect of these changes on the vertebral column as a whole will then be considered.

The relationship of the disc to spinal deformities, such as the arthritides, kyphoses, tumors and injuries will also be discussed.

COURSE: 213

Room: 403 **Period: T-2**

C. G. DYKE, M.D., New York City

The Normal Encephalogram and Ventriculogram

This seminar will deal with the history of pneumoencephalography, the indications and contraindications for the procedure, the reactions to the test, the preparation of the patient, and the roentgen technique. The discussion of the above subjects will be

followed by a thorough roentgen study of the lateral ventricles, the basal cisterns and the cortical markings, and also the structures which bound them. The demonstration will be illustrated.

COURSE: 214

Room: 403 Periods: W-2; Th-2

C. G. DYKE, M.D., New York City

Pneumo-encephalographic Diagnosis of Brain Tumor

This period will be devoted to an enumeration of the criteria used in the diagnosis of the various types of intracranial tumors. The characteristic changes produced by some of the neoplasms will be emphasized. The demonstration will be fully illustrated.

COURSE: 215

Room: 408 Period: T-2

PEDRO L. FARIÑAS, M.D., Havana, Cuba

Bronchographic Examination in Primary Bronchogenic Carcinoma

Description of technique.

Bronchographic aspects of the infiltrating and polypoid types of tumors.

Comparison between the bronchographic alterations and the anatomical specimen in the different types of bronchial tumors.

COURSE: 216

Room: 409 Period: T-2

JOHN T. FARRELL, JR., M.D., Philadelphia, Pa.

Roentgen Diagnosis of Lesions of the Esophagus

The technique of roentgen examination of the esophagus with liquids, semi-solids, and solids, together with the indications and limitations of each, will first be presented. This will be followed by consideration of the roentgen anatomy and physiology. Study of pathological states will embrace the diagnosis and differential diagnosis of congenital, inflammatory, traumatic, functional, and neoplastic conditions of the organ.

COURSE: 217

Room: 402 Period: W-2

A. O. HAMPTON, M.D., Boston, Mass.

Iodized Oil Myelography in the Diagnosis of the Prolapsed Intervertebral Disc

This course will deal chiefly with the diagnosis of ruptured intervertebral discs. The technique of examination, the sources of error and the mechanism of the filling defects produced by these lesions will be illustrated. Comparisons will be made between iodized oil myelography and air myelography in the diagnosis of ruptured discs.

COURSE: 218

Room: 401 Period: F-2

PAUL C. HODGES, M.D., Chicago, Ill.

Further Developments in Roentgen Pelvimetry and Fetometry with Special Reference to Orthometric Reproduction

The indications for roentgen pelvimetry and fetometry, the technique of making the measurements, and the application of the measurements to clinical obstetrics will be considered. Models, specimens, charts and roentgenograms will be demonstrated. Opportunity will be given for questions and discussion.

COURSE: 219

Room: 409 Period: F-2

B. R. KIRKLIN, M.D., Rochester, Minn.

Roentgenologic Appraisal of Results Following Operations on the Stomach and Duodenum

When surgical operations have been performed on the stomach and duodenum, roentgenologic examination is often solicited to determine whether satisfactory results have been obtained, or whether the original disease has recurred, or whether new complications have developed. Manifestly this field of diagnosis is difficult, for surgical techniques vary considerably both from choice and from necessity. Nevertheless, examination with the roentgen ray is the most readily available and most reliable method of exhibiting and appraising postoperative conditions. Accordingly, in this course of instruction the following subjects will be discussed in detail:

Preliminary information that should be given the roentgenologist—character of operation, disease for which it was performed, time that has elapsed since operation.

Technique of examination. Differences between early and late results. Satisfactory results from the various operations including gastrojejunostomy,

Billroth I, Billroth II, Polya, Roux, total gastrectomy, sleeve resection, local resection, pyloroplasty, gastroduodenostomy, entero-enterostomy.

Operations that appear roentgenologically to be most satisfactory in their mechanical and functional results.

Unsatisfactory results from operation. Complicating lesions including gastrojejunal ulcer, gastrojejunitis, gastro-jejuno-colic fistula and recurring ulcer.

COURSE: 220

Room: 403 **Period: W-3**

KARL KORNBLUM, M.D., Philadelphia, Pa.

Tumors about the Sella Turcica

The roentgen examination of the head with special reference to the sella turcica, emphasizing particularly the need of careful roentgenographic technique. The anatomy of the region of the sella turcica will be given and attention directed to the cardinal changes produced by tumors in its vicinity. The characteristic deformities occurring in the intrasellar, suprasellar and parasellar tumors and neoplasms arising in the sphenoid sinus will be considered.

COURSE: 221

Room: 406 **Period: Th-2**

A. S. MACMILLAN, M.D., Boston, Mass.

Roentgen Examination of the Accessory Nasal Sinuses

The technique of examination of the patient for suspected sinus disease will be considered. Particular stress will be placed upon four positions which the instructor considers the irreducible minimum in the examination of the sinuses.

Acute and chronic sinusitis, the sinus involvement in allergy and in malignant disease as well as the cause of exophthalmus in sinus involvement.

There is a great deal of discussion among otolaryngologists as to the value of the roentgen ray as an aid in the diagnosis. At attempt will be made to talk about the practical points in interpretation.

COURSE: 222

Room: 406 **Period: F-3**

A. S. MACMILLAN, M.D., Boston, Mass.

Roentgen Examination of the Mastoids

The technique of the examination of the patient for mastoid involvement in acute infections of the middle ear will be considered. Demonstrations of the various positions for the examination of the petrous pyramid in the search for involvement of this area as a complication of infection and invasions by new growths of the base of the skull and nasopharynx.

He will consider the rôle played by the roentgen ray in the determining of the optimum time for operation, the limitations of this type of examination and the need for the roentgenologist to acquaint himself with the problems of the surgeon.

COURSE: 223

Room: 414 **Period: Th-2**

B. H. NICHOLS, M.D., Cleveland, Ohio

Diagnosis of Renal Tumors

This instruction course will consist of a classification of renal tumors with a discussion of many of their clinical features which might lead to the supposition of the presence of such a lesion. There will also be presented the characteristic roentgen findings in the various types of tumors, together with lesions simulating renal tumors, with their differential diagnosis.

COURSE: 224

Room: 408 **Period: Th-2**

CARLETON B. PEIRCE, M.D., Montreal, Canada

Bronchographic Technique with Demonstration of the Anatomy and Pathologic Changes of the Bronchial Tree

The preparation of the patient for bronchography, the apparatus used and the various techniques for instillation of iodized oils will be demonstrated and discussed briefly.

Major emphasis will be placed on the demonstration of the topography of the normal bronchial tree, the localization and diagnosis of pathologic changes of the trachea and bronchi.

COURSE: 225

Room: 406 **Period: W-3**

JOHN W. PIERSON, M.D., Baltimore, Md.

Bone Changes in Lymphoblastomata

The roentgenological study of the skeletal manifestations of the lymphoblastomata is of interest because the bone changes assume so many and such varied forms. In some cases gross deformities of bone are produced, while in others the changes are so minimal that they are extremely difficult to detect.

This great variety of changes renders the differential diagnosis exceedingly difficult, because many other conditions are imitated. A review of the pathological background offers a logical explanation for the changes depicted by roentgen examination.

The gross changes are easy to demonstrate but signs of early involvement of the bones are extremely difficult to detect. Success in the demonstration of minimal changes can only be obtained by painstaking efforts in which a very precise technique is employed. Such a technique will be discussed and its results demonstrated.

COURSE: 226

Room: 403 **Period: F-2**

LEO G. RIGLER, M.D., Minneapolis, Minn.

Roentgen Diagnosis of Pleural Effusions

The anatomy, physiology and physical characteristics of the pleura and pleural space will be reviewed. The importance of these factors in the roentgen consideration of pleural collections will be emphasized. Early diagnosis and differential diagnosis of fluids in the pleural cavity, free and encapsulated, will be reviewed. The differential findings exhibited by exudates and transudates and encapsulated collections will be demonstrated. Roentgenologic findings in pneumothorax and its complicated aspects such as adhesions, encapsulations, fluid and mediastinal hernia will be detailed. The technique of the roentgenoscopic and roentgenographic examination of the pleural cavity for disease will be considered.

COURSE: 227

Room: 403 **Period: F-3**

SAMUEL A. ROBINS, M.D., Boston, Mass.

Utero-salpingography

This course concerns itself with the roentgen examination of the uterus and tubes by means of opaque media. The subject will be discussed under the following headings: (1) history; (2) apparatus and technique; (3) opaque media; (4) indications; (5) normal morphology; (6) physiologic variations; (7) pathologic variations; (8) pregnancy; (9) tumors (fibroids, polypi, malignancy); (10) inflammatory changes of the tubes; (11) tubal pregnancy; (12) sterility; (13) post-therapeutic changes in the uterus; (14) contraindications; (15) dangers.

Lantern slides of various physiologic and pathologic conditions of the uterus and tubes will be shown to evaluate this method of examination.

COURSE: 228

Room: 405 **Period: W-3**

L. R. SANTE, M.D., St. Louis, Mo.

Bronchial Occlusion

Tracheal obstruction
Roentgen manifestations and causes
Complete bronchial obstruction resulting in atelectasis: massive type from obstruction of main stem bronchus; lobar form from occlusion of larger bronchial branches; lobular form resulting from occulusion of smaller bronchial subdivisions.

The causes and conditions which give rise to these various types of bronchial occlusion; their association with other conditions and diseases such as aspiration of foreign body, trauma, pulmonary tuberculosis, bronchogenic tumor, postoperative inhibition, general debility, weakness, etc.

Incomplete bronchial occlusion resulting in obstructive emphysema: massive involvement of entire lung (Manges' sign), smaller bronchial subdivisions, bronchiectasis and pseudobronchiectasis from partial bronchial obstruction by foreign body of long sojourn and from bronchogenic tumor.

COURSE: 229

Room: 407 **Periods: W-3; F-3**

RICHARD SCHATZKI, M.D., Boston, Mass.

Roentgen Diagnosis of Gastritis

Over-emphasis and marked criticism characterize the present attitude towards roentgen diagnosis of gastritis. This course tries to evaluate critically our knowledge at this time. Its emphasis is laid upon the practically important features connected with the diagnosis and differential diagnosis of gastritis, and not on theoretical considerations. The reasons why, in spite of the progress of gastroscopy, gastritis is still a problem for everyday roentgenology will be illustrated.

The round table discussion will include the following questions:

General principle and technique of the gastric relief demonstration; roentgen findings in some types of gastritis; critical discussion of the possibilities and limitations in regard to roentgenological diagnosis of gastritis; differential diagnosis.

COURSE: 230

Room: 410 **Period: Th-2**

W. H. STEWART, M.D., New York City
FRANK HUBER, M.D., New York City

Lesions of the Lower Esophagus and Cardiac Portion of the Stomach

A discussion of the recognition and differential diagnosis of lesions of the lower esophagus and cardiac portion of the stomach.

Carcinoma, diverticula, cardiospasm, peptic ulcer, varices, diaphragmatic hernia, congenitally short esophagus, as well as carcinoma and diverticula of the cardiac portion of the stomach will be discussed

and illustrated. In addition to the examples showing characteristic involvement, films will be shown of atypical lesions offering unusual diagnostic difficulties.

The presentation will include an outline of the positions and technique necessary to obtain diagnostic films as well as some discussion of therapeutic procedures.

COURSE: 231

Room: 414 **Period: W-2**

M. S. STROCK, D.M.D., Boston, Mass.

Analysis of Dental Roentgenograms as an Aid in the Recognition of Systemic Disease

This seminar will correlate dental findings as seen in the regular dental film with systemic disease, particularly with disorders of the calcium and phosphorus metabolism. An effort will be made to show from dental films the everyday pathology as well as some of those diseases which, though rare, manifest themselves in the mouth. Particular attention will be given to hyperparathyroidism and hypoparathyroidism and their oral manifestations. The need for accurate dental findings will be pointed out, yet an attempt will be made to keep the description of findings sufficiently brief to be of value in the hospital.

COURSE: 232

Room: 400 **Periods: W-3; F-3**

PAUL C. SWENSON, M.D., New York City

Neoplasms of the Small Intestine

The incidence and character of the various benign and malignant neoplasms of the small intestine, including those of the duodenum, will be discussed. The roentgenologic manifestations of these lesions will be presented, and the technique of examination, including the use of the Miller-Abbott tube, will be described in detail.

COURSE: 233

Room: 407 **Period: F-2**

KURT H. THOMA, D.M.D., Boston, Mass.

Changes in the Jaws caused by Skeletal Diseases and Tumors

The roentgen and pathologic findings of various lesions of the jaw will be shown, and the clinical findings will be described. The proper roentgen method for lesions located in various parts will be discussed. The following diseases will be considered:

1. Fractures of the jaws.
2. Diseases of the mandibular joint.
3. Skeletal diseases: cretinism, acromegaly, hyperparathyroidism, osteitis deformans, Schüller-Christian's disease, osteosclerosis fragilis generalisata.
4. Localized diseases: oxycephaly, leontiasis ossea, atrophy, hemiatrophy, osteomyelitis, irradiation osteomyelitis, syphilis.
5. Cysts of the jaws: facial cleft cysts, incisive canal cysts, odontogenic cysts, traumatic cysts.
6. Odontogenic tumors: adamantinomoblastoma, odontoma, cementoma.
7. Osteogenic tumors: exostosis (torus palatinus), osteoma, chondroma, myxoma, osteogenic sarcoma.
8. Central tumors of non-odontogenic and non-osteogenic origin: fibroma and fibrosarcoma, angioma, Ewing's tumor, multiple myeloma, primary carcinoma, and tumors metastatic to the jaws.

COURSE: 234

Room: 406 **Period: F-2**

EDWARD C. VOGT, M.D., New Bedford, Mass.
GEORGE M. WYATT, M.D., Boston, Mass.

Chest and Heart Diseases in Infants and Children

We arbitrarily divide our patients into two age periods, namely, infants from birth to two years, and children from two years to twelve, because there is a certain age incidence in the diseases encountered. Also because certain diseases, such as tuberculosis, are less easily differentiated in early years of life. Diseases of congenital origin are more likely encountered in the infant. This is particularly true of heart disease. Using lantern slide illustrations we will discuss with as much detail as our time permits the different disease conditions, primary and secondary, congenital and acquired, that affect the heart, lungs, pleura, mediastinum and thorax.

COURSE: 235

Room: 407 **Periods: T-2; W-2**

W. WALTER WASSON, M.D., Denver, Colorado

The Nasal Accessory Sinuses of Infants

This presentation has to do particularly with aeration of the nasal accessory sinuses of infants after delivery. This clearing process is a definite physiological one and has many variations. Improper clearing soon becomes a pathologic condition and a basis for future sinus infections. These sinus infections definitely influence the entire respiratory tract.

COURSE: 236

Room: 406 **Period: W-2**

HARRY M. WEBER, M.D., Rochester, Minn.

Lesions of the Colon Frequently and Easily Overlooked

Advanced pathologic processes occurring in the large intestine usually produce relatively marked morphologic changes in the part of the intestine affected, and so are discovered without great difficulty at roentgenologic examination. Certain clinically important lesions, however, never become large, or produce alarming symptoms even when small, or are encountered so early in their development that very obvious morphologic changes have not as yet taken place, and thus are easily overlooked at roentgenologic examination. This discussion will be limited to the roentgenologic diagnosis of small neoplastic lesions of the large intestine, and to those roentgenologically recognizable changes which signify the earliest manifestations of certain important non-neoplastic lesions of this division of the alimentary tract. The conduct of the roentgenologic examination of the large intestine will be reviewed briefly, and advantages and limitations of the various diagnostic procedures currently used in this field will be discussed in considerable detail.

SINGLE PERIOD COURSES

THERAPEUTIC RADIOLOGY

COURSE: 301

Room: 410 **Period: T-2**

ARTHUR U. DESJARDINS, M.D., Rochester, Minn.

Lymphoblastoma (Hodgkin's Disease, Lymphosarcoma and Leukemia)

Prominent clinical features of Hodgkin's disease and lymphosarcoma; presenting symptoms and their relative importance; involvement of mediastinal nodes; involvement of retroperitoneal nodes; involvement of other nodes; extranodular infiltration; involvement of skin; great variation in complications; pathology; condition of the blood; treatment in relation to anatomic distribution of the disease and of its complications; quantity and quality of rays; variations in radiosensitiveness and reasons therefor; effect on the blood cells; repetition of treatment and factors which should govern it; prognosis; factors governing survival.

COURSE: 302

Room: 410 **Periods: W-3; F-3**

RICHARD DRESSER, M.D., Boston, Mass.

Roentgen and Radium Therapy

This course will be prefaced by a brief résumé in simple terms of the physical principles of radiation. The effect of voltage, filtration, distance, etc., in roentgen-ray production will be discussed. The relative merits of various methods of radium application will be taken up.

The radiological management and end-results in the more common types of malignant disease will be discussed. Special attention will be given to cancer of the skin, lip, mouth, larynx, breast, uterus, bladder, and prostate.

The advantages and limitations of roentgen rays produced at voltages greater than 200,000 will be given brief consideration.

COURSE: 303

Room: 405 **Period: T-2**

E. C. ERNST, M.D., St. Louis, Mo.

Practical Concepts of Radiation Treatment of Carcinoma of the Cervix Uteri

The practical irradiation management of carcinoma of the cervix will be discussed both from the standpoint of the institutional tumor clinic and the private office procedure. Although realizing that the radiation treatment standards continue to remain somewhat in a state of flux and that individualization in the application of roentgen rays and radium is a most essential consideration, nevertheless certain fundamental concepts in our routine procedures are most helpful in the management of cancer of the cervix. These and many other practical therapeutic considerations, including external roentgen therapy, intracavity radium and roentgen methods of treatment and the dosage measurement problems, will be discussed and illustrated.

COURSE: 304

Room: 413 **Period: F-3**

G. FAILLA, D.Sc., New York City

Some Aspects of Radiosensitivity

Variation of radiosensitivity with cell type, stage of development, etc.

Influence of circulation on cell reaction to radiation in accordance with author's theory of the biological action of ionizing radiations. Experimental findings tending to support theory.

Relative radiosensitivity of normal and pathological tissues most important factor in radiation ther-

apy. Ways in which radiosensitivity ratio may be improved. Possible influence of wave length on this ratio.

Applications to some practical problems.

COURSE: 305

Room: 413 **Period: F-2**

ROBERT E. FRICKE, M.D., Rochester, Minn.

Radiation Therapy for Carcinoma of the Rectum

Carcinoma of the rectum presents many problems not encountered in malignant disease elsewhere in the body. In early stages it is best handled surgically. However, very few rectal lesions are diagnosed in an early stage. Radiation therapy has a major rôle in this disease in close conjunction with surgical measures. For the past several years between 100 and 200 patients with carcinoma of the rectum have received radium therapy each year at the Mayo Clinic, some postoperatively, a few preoperatively, and the majority with advanced inoperable lesions were treated with palliation in mind. Results of treatment have been definitely encouraging. Roentgen therapy has been helpful in selected cases.

Newer methods of radiation treatment will be described. The microscopic grade of the cancer, its location, the presence or absence of metastasis and the general condition of the patient all have an important bearing on the selecting of the type of treatment. Topical or contact therapy and interstitial treatment with needles or seeds will be described. The advantages and disadvantages of colostomy will be mentioned. Results of treatment will be given and a discussion of the value of the palliation offered by treatment in inoperable cases. At the present time radiation therapy has a major rôle in the palliative treatment of extensive inoperable lesions; in the future I believe preoperative therapy will prove even more successful and applicable in the management of these serious conditions.

COURSE: 306

Room: 414 **Period: F-2**

OTTO GLASSER, Ph.D., Cleveland, Ohio
U. V. PORTMANN, M.D., Cleveland, Ohio

Dosage Measurements with the Thimble Chamber in Practice

The historical development of thimble chamber dosimeters, their calibration in roentgens, the measurement of quantity and quality, depth dose and back-scattering in phantoms will be discussed. The difference between the thimble chamber dosimeters and other types of dosimeters will be discussed. Likewise, the clinical applications of the thimble chamber will be discussed.

COURSE: 307

Room: 412 **Period: T-2**

GEORGE W. GRIER, M.D., Pittsburgh, Pa.

Treatment of Superficial Malignant Neoplasms

A general outline of the technique which the author has used for treatment of superficial malignant neoplasms since the advent of the Coolidge tube will first be given.

Variations in technique for lesions in different locations and different types of involvement will be discussed. Also, variations which are necessary in different types of malignant disease.

The actual application of masks and special applicators which may be necessary in difficult locations will be demonstrated.

Lesions of the lip and mouth will be included.

Abstracts of actual case histories with illustrative lantern slides will be presented for each type of lesion described.

COURSE: 308

Room: 408 **Period: F-2**

ARTHUR U. DESJARDINS, M.D., Rochester, Minn.

Roentgen Treatment of Inflammatory Conditions

This instructor will discuss the roentgen treatment of the following conditions: furunculosis, carbuncle, granuloma, erysipelas, gas bacillus infection, mastoiditis, sinusitis, osteomyelitis, some fungus infections, various localized types of cellulitis, infected rhinophyma, bronchiectasis, etc. The dosage and technique will be discussed in detail.

COURSE: 309

Room: 408 **Period: W-2**

H. DABNEY KERR, M.D., Iowa City, Iowa

Roentgen Irradiation of Deep Pelvic Malignant Tumors, Particularly Carcinoma of the Cervix

Although standardized methods of treatment are valuable, it is important to know what is actually being delivered to the lesion, and the response, if we are to make any real advance in our irradiation of pelvic neoplasms. This will be a discussion of the method used in the treatment mainly of carcinoma of the cervix at the University of Iowa. Where possible this consists of the use of nine portals about the pelvis and, in addition, either radium or transvaginal roentgen irradiation according to the method advocated by Merritt and by Erskine. The question of doses delivered to the parametrial extensions and the primary lesion will be discussed in relation to daily dosage division and cumulative dose. An attempt

will also be made to correlate delivered dose with clinical result.

COURSE: 310

Room: 412 **Periods: W-3; F-3**

MAURICE LENZ, M.D., New York, N. Y.

Roentgen Therapy of Cancer of the Larynx and Pharynx

Roentgen therapy of cancer of the larynx and pharynx is influenced by the clinical character, anatomical extent and location, accessibility, invasion of cartilage or bone, infection, ability of the patient to tolerate radiotherapy, and inherent radiosensitivity of the tumor. Technique of treatment also has an important bearing upon prognosis.

All the patients with cancer of the larynx and pharynx treated in the Radiotherapy Departments of Presbyterian Hospital and Montefiore Hospital, New York City, between 1926 and 1939 (approximately 250 cases) have been analyzed in an effort to clarify the relative importance of the factors just mentioned. This analysis, together with data in the literature, forms the basis of this informal discussion. It is hoped that a free interchange of views on details of the problem will take place between lecturer and audience during the course.

COURSE: 311

Room: 414 **Periods: W-3; F-3**

T. LEUCUTIA, M.D., Detroit, Mich.

Radiation Therapy of Bone Tumors

(1) Osteogenic sarcoma. Radiation therapy is used in association with surgery in pre- or postoperative form in all types, except the pure osteolytic type, in which it is used alone. In the inoperable group, irradiation produces definite symptomatic relief. The five year survival for the entire series amounts to 17 per cent.

(2) Giant cell tumor. Here radiation therapy is the method of choice. There are two requisites: (*a*) irradiation must be carried out with gradually decreasing doses for nearly two years, and (*b*) a limited use of the affected bone must be made so as to prevent marked demineralization from disuse. The final results are, with few exceptions, good.

(3) Ewing's tumor. In the very early cases, radiation therapy may lead to occasional five year survival; in the others, only palliation is obtained, although the immediate response is often striking.

(4) Multiple myeloma. Radiation therapy leads to limited symptomatic relief, but no cure is possible.

(5) In the group of benign tumors, radiation therapy is of definite value in chondroma, myxoma, hemangioma, cystic conditions, etc.

The detailed procedure is presented in the various groups and the technique of irradiation illustrated. Final statistical data are included.

COURSE: 312

Room: 410 **Period: F-2**

CHARLES L. MARTIN, M.D., Dallas, Texas

Complete Care of Cancer of Mouth and Lip Including Cervical Metastases with Irradiation Alone

A plan for the complete radiological care of all stages of cancer of the mouth and lip will be described. Although both radium and roentgen rays are used, the equipment is relatively inexpensive and the time of treatment is short. Much emphasis will be placed on the intensive irradiation of metastatic cervical glands, using a combined roentgen-ray and interstitial radium technique which has yielded some very promising results. Detailed descriptions of the procedure used in a number of actual cases have been prepared for presentation.

COURSE: 313

Room: 405 **Periods: Th-2; F-2**

E. A. MERRITT, M.D., Washington, D. C.

Technique of Treatment of Cancer of the Cervix and Results Therefrom

This presentation is intended neither as a lecture nor as an instruction course; however, it embraces a complete description of a technique covering the radiation treatment of all stages of carcinoma of the cervix uteri.

The advantages of roentgen over radium therapy will be emphasized and a method of treating the cancerous cervix through specially designed specula will be described.

Hospitalization of the patient is rarely necessary, infection is reduced to a minimum; anesthetics and surgical trauma of the cervix completely avoided; severe roentgen sickness and undue skin reactions almost completely controlled.

It provides the radiologist with a standardized technique which will facilitate future statistical comparisons, and divorces therapy of cancer of the cervix from all of the unnecessary and expensive surgical procedures and dangers associated with the use of radium.

Lantern slides, a wax model, and specula employed will serve to clearly demonstrate the method in actual operation.

Results covering a three year period will be stated.

COURSE: 314

Room: 412 **Period: F-2**

WILLIAM S. NEWCOMET, M.D., Philadelphia, Pa.

Radium Therapy of Hemangiomata

Early methods used in the treatment of hemangiomata.

The application of roentgen and radium radiation, the differences between them.

Varieties of hemangiomata from the standpoint of the pathologist, dermatologist, surgeon and radiologist.

Possibility of malignant degeneration in those treated by irradiation and those of unknown origin, in youth and adult life.

Spontaneous ulceration and ulceration occurring during treatment. Other complications, local lack of growth, dermatitis local and general, telangiectasis and lack of function of affected part.

Discussion of treatment in the young infant, child and adult.

General review of groups and individual cases; with emphasis upon unusual bone changes observed in different types.

Results observed immediately after treatment and ten to twenty years later.

COURSE: 315

Room: 405 **Periods: W-2; F-3**

G. E. PFAHLER, M.D., Philadelphia, Pa.

Radiation Treatment of Cancer of the Breast

The technique for the treatment of cancer of the breast cannot be standardized. The treatment will be demonstrated for cancer of the breast in various stages, including positioning of patient for treatment.

There will also be a demonstration of some of the cases treated primarily and completely by irradiation, also preoperative and postoperative irradiation, including the management of recurrences.

COURSE: 316

Room: 414 **Period: T-2**

U. V. PORTMANN, M.D., Cleveland, Ohio

The Thyroid Gland, Its Anomalies and Diseases

The embryology, anatomy and physiology of the thyroid gland will be discussed in relationship to the etiology and treatment of pathological conditions such as anomalies, diseases attributed to dysfunction and neoplasms.

COURSE: 317

Room: 402 **Period: Th-2**

DOUGLAS QUICK, New York City

Treatment of Metastatic Cervical Nodes from Primary Epidermoid Carcinoma of the Upper Mucous Membrane Tract

The problem will be considered under the following headings:

1. General considerations leading up to the present plan.
2. External irradiation, its place, and technical manner of delivery.
3. Surgical dissection of the neck.
4. Interstitial irradiation, preferential method, and technique.
5. Palliative therapy.

COURSE: 318

Room: 408 **Period: W-3**

EDITH H. QUIMBY, M.S., New York City

Artificial Atomic Disintegration

This course will be essentially a general descriptive outline of methods of producing atomic disintegration, and of the products thus obtained. Neutrons and artificially radioactive substances will be discussed in some detail. Brief mention will be made of various biological and clinical uses to which these materials have been put, up to the present time.

COURSE: 319

Room: 410 **Period: W-2**

GORDON E. RICHARDS, M.D., Toronto, Canada

The Treatment of Carcinoma of the Tongue and Buccal Mucosa

The material for this course is based on a careful study of approximately 200 cases of carcinoma of the tongue in which the primary lesion has been treated by irradiation. The irradiation procedures have included radium in a variety of forms from weak seeds to teleradium therapy with a 4 gram radium bomb, and roentgen therapy at all voltages from the Chaoul method to 400 kv. therapy. Complications have been treated both by irradiation and by combinations of surgery and radiotherapy. The cases are thoroughly worked up and certain decisions have been reached which have been agreed to by surgical consultants. The results in this series of cases are distinctly encouraging and I think we are in a position to make quite definite statements on most of the important problems which arise in treating carcinoma of the tongue.

The group of cases of carcinoma of the buccal mucosa is smaller. These cases have also been carefully worked up and here, likewise, we have reached conclusions which are encouraging and are somewhat at variance with present day teaching regarding this disease.

COURSE: 320

Room: 413 **Period: T-2**

K. W. STENSTROM, Ph.D., Minneapolis, Minn.

Characteristic Roentgen Radiation and Absorption

1. Introduction:
   Wave length of roentgen rays. Spectrometric analysis of a roentgen-ray beam. Graphic representation of the continuous spectrum. Consideration of photons, quanta. The atomic structure.
2. Characteristic radiation produced in the target of the roentgen tube.
3. Groups of spectral lines from tungsten, K, L, M lines.
4. Characteristic radiations from the different elements and their correlation with atomic numbers.
5. Absorption of roentgen rays by atoms.
6. Characteristic absorption.
7. Characteristic radiation produced by roentgen rays.
8. Selection of secondary filters.

COURSE: 321

Room: 413 **Period: Th-2**

ROBERT B. TAFT, M.D., Charleston, S. C.

Dosage Measurement from a Clinical Standpoint

The author proposes to describe briefly and show photographs of all the methods in use today for roentgen-ray measurement, stating the advantages and disadvantages of each. Illustrations should be obtainable from manufacturers, which will be shown as lantern slides. The value of the "roentgen" as a clinical unit will be discussed and mention of the proposed unit, the "duane" will be made. Pros and cons for the direct dosage measurement on the skin of the patient throughout the treatment time will be given. Air measurements versus skin measurements will be outlined and tables given for back-scattering at commonly used wave lengths. Half of the period will be taken up with the above and round table discussion will follow. Throughout all, an earnest effort will be made to keep the matter within the scope of the clinical radiologist who has little knowledge of, or interest in, pure physical measurements. The author, having had some experience in both clinical and physical work, will attempt to narrow the far-too-wide gap between the clinician and physicist. A typed summary will be available to those attending.

COURSE: 322

Room: 413 **Period: W-2**

LAURISTON S. TAYLOR, Ph.D., Washington, D. C.

The Measurement of Quantity and Quality of Roentgen Rays

A general discussion, aimed at showing the necessity for roentgen-ray quantity and quality measurements, will be presented. A brief outline of the fundamental principles involved in the application of roentgen-ray standards will be given. A few examples of actual cases involving the application of physical dosage measurement will be carried through. Likewise the method of determining an absorption curve will be illustrated and the information obtainable therefrom discussed. No discussion of tissue dosage or related subjects will be given.

COURSE: 323

Room: 412 **Period: W-2**

CHARLES A. WATERS, M.D., Baltimore, Md.

Radiation Treatment of Renal Tumors

The author will discuss (1) a brief differential diagnosis of renal tumors as related to roentgen diagnosis and treatment; (2) previous statistics on the curability of renal tumors without the aid of preoperative irradiation; (3) the immediate effects of radiation upon the various types of renal tumors; (4) the dangers, pitfalls, and contraindications of irradiation; (5) a discussion of elapsed time between the radiation therapy and operative removal, and (6) the results in preoperative irradiated cases as compared to non-preoperative irradiated cases.

COURSE: 324

Room: 407 **Period: Th-2**

J. L. WEATHERWAX, M.S., Philadelphia, Pa.

Radium Dosage

A brief discussion of the disintegration cascade of radium; active deposit; differentiation of radium compared to radium emanation or radon; absorption by different filters and thicknesses of filter; half-life and average life of radon; types of radium applicators; interstitial irradiation; expression of dosage in terms of milligram-hours, millicurie-hours; millicuries-destroyed and a discussion of an attempt to express dosage in roentgens.

An outline will be furnished with a bibliography.

COURSE: 325

Room: 409 **Periods: W-3; F-3**

B. P. WIDMANN, M.D., Philadelphia, Pa.

Radiation Therapy in Cancer of the Skin

Technical procedures for the radium and roentgen treatment of cancer of the skin will be reviewed and analyzed in detail. A definite predetermined plan of dosage has been formulated according to the estimated surface area and thickness of the lesion. Special emphasis will be placed on the value of low voltage roentgen rays (100–135 kv.), and a clinical comparison with radium will be made according to a great variety of patterns for single and multiple radium tubes with different sizes of fields, filters and distances. Conclusions will be drawn from a large clinical experience with massive and fractional doses. Determinations of the "maximum safe dose," the "minimal effective dose," the daily intensity and the probable best rate of administration will be considered with specific recommendations after a routine experience demonstrating results and skin tolerance.

CONDENSED SCHEDULE OF COURSES ON TUESDAY

Code: T-1 **1st PERIOD—2:00 to 2:50** **Code: T-1**

SL-1....Warren.....Special Lecture: Radiosensitivity of Tumors

Code: T-2 **2nd PERIOD—3:00 to 4:15** **Code: T-2**

Diagnostic Roentgenology		Therapeutic Radiology and Sequential Courses	
203—Bishop	Examination and Diagnosis of Lesions of Temporomandibular Joint	**A—Murphy**	Bone Tumor Conference
207—Case	Roentgenologic Diagnosis of Cancer of the Colon	**301—Desjardins**	Lymphoblastoma
209—Christie	Diagnosis and Treatment of Bronchiectasis	**303—Ernest**	Radiation Treatment of Cancer of the Cervix
213—Dyke	Normal Encephalogram and Ventriculogram	**307—Grier**	Treatment of Superficial Malignant Neoplasms
215—Fariñas	Bronchographic Diagnosis of Primary Bronchogenic Carcinoma	**316—Portmann**	The Thyroid Gland
216—Farrell	Roentgen Diagnosis of Lesions of the Esophagus	**320—Stenstrom**	Characteristic Roentgen Radiation and Absorption
235—Wasson	Nasal Accessory Sinuses of Infants		

CONDENSED SCHEDULE OF COURSES ON WEDNESDAY

Code: W-1 **1st PERIOD—2:00 to 2:50** **Code: W-1**

SL-2....Schnelle.....Special Lecture: Roentgen Rays in Veterinary Medicine

Code: W-2 **2nd PERIOD—3:00 to 4:15** **Code: W-2**

Diagnostic Roentgenology		Therapeutic Radiology and Sequential Courses	
205—Butler	Fractures from their Medico-legal Standpoint	**A—Murphy**	Bone Tumor Conference
209—Christie	Diagnosis and Treatment of Bronchiectasis	**309—Kerr**	Roentgen Treatment of Deep Pelvic Neoplasms
214—Dyke	Pneumo-encephalographic Diagnosis of Brain Tumors	**315—Pfahler**	Radiation Treatment of Cancer of the Breast
217—Hampton	Iodized Oil Myelography in Diagnosis of Protruded Intervertebral Disc	**319—Richards**	Treatment of Carcinoma of the Tongue and Buccal Mucosa
231—Strock	Analysis of Dental Roentgenograms as Aid in Recognizing Systemic Disease	**322—Taylor**	Measurement of Quantity and Quality of Roentgen Rays
235—Wasson	Nasal Accessory Sinuses of Infants	**323—Waters**	Radiation Treatment of Renal Tumors
236—Weber	Lesions of the Colon Easily and Frequently Overlooked		

Code: W-3 **3rd PERIOD—4:30 to 5:45** **Code: W-3**

Diagnostic Roentgenology		Therapeutic Radiology and Miscellaneous Courses	
202—Archer Bogart	Chest Findings in "Country Diseases"	**102—Henny**	Roentgen Film Characteristics and Calibration of Apparatus and Developing Solutions
212—Doub	The Intervertebral Disc	**302—Dresser**	Roentgen and Radium Therapy
220—Kornblum	Tumors about the Sella Turcica	**310—Lenz**	Roentgen Therapy in Cancer of the Larynx and Pharynx
225—Pierson	Bone Changes in Lymphoblastoma	**311—Leucutia**	Radiation Therapy in Tumors of Bone
228—Sante	Bronchial Occlusion	**318—Quimby**	Artificial Atomic Disintegration
229—Schatzki	Roentgen Diagnosis of Gastritis	**325—Widmann**	Radiation Therapy in Cancer of the Skin
232—Swenson	Neoplasms of the Small Intestine		

CONDENSED SCHEDULE OF COURSES ON THURSDAY

Code: Th-1 **1st PERIOD—2:00 to 2:50** **Code: Th-1**

SL-3....Castle.....Special Lecture: Leukemia

Code: Th-2 **2nd PERIOD—3:00 to 4:15** **Code: Th-2**

Diagnostic Roentgenology	
204—Bromer	Differential Diagnosis of Skeletal Changes in Diseases of Children
211—Cole	Pneumoconiosis
214—Dyke	Pneumo-encephalographic Diagnosis of Brain Tumors
221—Macmillan	Roentgen Examination of the Accessory Nasal Sinuses
223—Nichols	Diagnosis of Renal Tumors
224—Peirce	Bronchographic Demonstration of Anatomy and Pathology of Bronchial Tree
230—Stewart Huber	Lesions of Lower Esophagus and Cardiac Portion of Stomach

Therapeutic Radiology, Miscellaneous and Sequential Courses	
A—Murphy	Bone Tumor Conference
101—George	Roentgenologist in Industrial Medicine. Roentgenologist as an Expert Witness
313—Merritt	Technique of Treatment of Cancer of Cervix and Results Therefrom
317—Quick	Radiation Treatment of Neck Metastasis
321—Taft	Dosage Measurement from a Clinical Standpoint
324—Weatherwax	Radium Dosage

CONDENSED SCHEDULE OF COURSES ON FRIDAY

Code: F-1 **1st PERIOD—2:00 to 2:50** **Code: F-1**

SL-4 . . . . **Albright** . . . . . Special Lecture: Osteoporosis

Code: F-2 **2nd PERIOD—3:00 to 4:15** **Code: F-2**

Diagnostic Roentgenology		Therapeutic Radiology	
208—Chamberlain	Technique and Interpretation of Oxygen Myelography	**305—Fricke**	Radiation Therapy in Carcinoma of the Rectum
210—Codman Blackett	The Shoulder	**306—Glasser Portmann**	Dosage Measurements with Thimble Chamber: Practical Applications
218—P. C. Hodges	Roentgen Pelvimetry and Fetometry; Orthometric Reproduction	**308—Desjardins**	Roentgen Treatment of Inflammatory Conditions
219—Kirklin	Stomach and Duodenum after Operation: Roentgenologic Findings	**312—Martin**	Radiation Treatment of Cancer of Lip and Mouth, including Cervical Metastasis
226—Rigler	Roentgen Diagnosis of Pleural Effusions	**313—Merritt**	Technique of Treatment of Cancer of Cervix and Results Therefrom
233—Thoma	Diseases and Tumors of the Jaw	**314—Newcomet**	Radium Therapy of Hemangiomata
Vogt 234—Wyatt	The Heart and Lungs in Children		

Code: F-3 **3rd PERIOD—4:30 to 5:45** **Code: F-3**

Diagnostic Roentgenology		Therapeutic Radiology	
201—Archer	Roentgen Manifestations in Osteomyelitis	**302—Dresser**	Roentgen and Radium Therapy
204—Bromer	Differential Diagnosis of Skeletal Changes in Diseases of Children	**304—Failla**	Some Aspects of Radiosensitivity
206—Carty	Soft Tissue Roentgenography	**310—Lenz**	Roentgen Therapy in Cancer of the Larynx and Pharynx
222—Macmillan	Roentgen Examination of the Mastoids	**311—Leucutia**	Radiation Therapy in Tumors of Bone
227—Robins	Utero-salpingography	**315—Pfahler**	Radiation Treatment of Cancer of the Breast
229—Schatzki	Roentgen Diagnosis of Gastritis	**325—Widmann**	Radiation Therapy in Cancer of the Skin
232—Swenson	Neoplasms of the Small Intestine		

AMERICAN RADIUM SOCIETY

The Twenty-fifth Annual Meeting of the American Radium Society will be held in New York City at the Hotel Waldorf Astoria on Monday and Tuesday, June 10 and 11, 1940. The following is the program which has been arranged:

PROGRAM

Monday, June 10, 1940

Morning Session (Empire Room)

8:30 A.M. Executive Session
9:00 A.M. Scientific Session

1. Presidential Address. Lawrence A. Pomeroy, M.D., Cleveland, Ohio
2. The Need for Clinical Classification of Cancer. Peter A. Nelson, M.D., Chicago, and Herbert E. Schmitz, M.D., Chicago (by invitation).
3. Treatment of Large Subcutaneous Hemangiomas with Removable Platinum Implants. Milton Friedman, M.D., New York City.
4. The Radium Treatment of Angiomas. Frank E. Simpson, M.D., and J. Ernest Breed, M.D., Chicago.
5. Pulmonary Lesions in the Lymphomas. Lloyd F. Craver, M.D., New York City.
   Discussion: James Ewing, M.D., and Ernst A. Pohle, M.D.

Intermission, 10 minutes

6. The Treatment of Leukoplakia Buccalis and Related Lesions with the Sex Hormones. Ira T. Nathanson, M.D., and David G. Weisberger, M.D., Boston (by invitation).
7. Carcinoma of the Penis. Louis H. Jorstad, M.D., St. Louis, Missouri (by invitation).
8. The Treatment of Cancer of the Rectum. George S. Sharp, M.D., Pasadena, California.
   Discussion: C. P. Rhodes, M.D., Archie L. Dean, M.D., and George E. Binkley, M.D.

Monday, June 10, 1940

Afternoon Session (Empire Room)

2:00 P.M. Executive Session
2:20 P.M. Scientific Session

Chairman, Frederick W. O'Brien, M.D., Boston

9. The Treatment of Cervical Metastatic Cancer. Hayes E. Martin, M.D., New York City.
10. Complications Following Irradiation of Breast Cancer. Joseph H. Farrow, M.D., New York City (by invitation).
11. Irradiation Pulmonary Fibrosis. Bernard P. Widmann, M.D., Philadelphia.
    Discussion: Charles L. Martin, M.D., Frank E. Adair, M.D., and Harriet C. McIntosh, M.D.

Intermission, 20 minutes

4:00 P.M. Janeway Lecture
The Specification of Dosage in Radium Therapy. Edith H. Quimby, M.A. Memorial Hospital, New York City.

Monday Evening, June 10, 1940

Annual Dinner

Hotel Waldorf Astoria—Sert Room
Reception and Apéritifs at Seven
Dinner at Eight
Remarks by the President
Presentation of The Janeway Medal to Edith H. Quimby, M.A.
Music—Dancing

Tuesday, June 11, 1940

Morning Session (Empire Room)

8:30 A.M. Executive Session
9:00 A.M. Scientific Session

Chairman, Hayes E. Martin, M.D., New York City

12. The Surgery of Post-irradiation Necrosis. Ernest M. Daland, M.D., Boston (by invitation).
13. Cancer of the Stomach in the Young. Gordon P. McNeer, M.D., New York City (by invitation).
14. Failures in Radiotherapy for Uterine Bleeding and Fibromyomata. James A. Corscaden, M.D., New York City.
15. Comments on the Treatment and Sequelae of Carcinoma of the Uterus. Elizabeth Newcomer, M.D., Denver, Colorado (by invitation).
    Discussion: Douglas Finch, M.D., George T. Pack, M.D., and Louis E. Phaneuf, M.D.

Intermission, 10 minutes

16. Carcinoma of the Uterine Cervix Treated with 400 kv. Roentgen Rays and Radium. John T. Murphy, M.D., and C. E. Hufford, M.D., Toledo, Ohio.
17. Analysis of 700 Cases of Carcinoma of the Cervix. Harold G. F. Edwards, M.D., Shreveport, Louisiana.
18. The Salvage in Vulvar and Cervical Cancer with Lymph Node Metastasis. Fred J. Taussig, M.D., St. Louis, Missouri.
19. Carcinoma of the Cervix Uteri in Childhood and Adolescence. A Review of the Literature and Report of an Additional Case of a Girl Aged Thirteen Years. Harry H. Bowing, M.D., and J. A. L. McCullough, M.D., Rochester, Minnesota.

    Discussion: Maurice Lenz, M.D., William P. Healy, M.D., and A. N. Arneson, M.D.

Tuesday, June 11, 1940

Afternoon Session

2:00 P.M. Executive Session

2:20 P.M. Scientific Session

Chairman, Eugene T. Leddy, M.D., Rochester, Minnesota

20. The Progress of Radium since its Earliest Therapeutic Availability. Albert Soiland, M.D., Los Angeles, California.
21. Radium Beam Therapy. Ira I. Kaplan, M.D., New York City.
22. The Experimental Modification of the Sensitivity of Yeast to Roentgen Rays. Robert S. Anderson, Ph.D., New York City.
23. The Influence of Radiation and Hibernation on Growth Behavior of Mouse Neoplasms. Henry J. Ullmann, M.D., Fritz Bishop, and Louisa Long, Santa Barbara, California.

    Discussion: Max Cutler, M.D., A. W. Oughterson, M.D., and Fred W. Stewart, M.D.
24. Some Considerations Regarding Induced Radioactivity. G. N. Glascoe, New York City (by invitation).
25. The Significance of Specific Ionization in the Biological Action of Various Radiations. Raymond E. Zirkle, Bryn Mawr, Pennsylvania (by invitation).
26. Protection of Personnel against Wide Therapy Beams of Roentgen and Gamma Rays. T. R. Folsom and B. Focht, New York City.

    Discussion: G. Failla, Edith H. Quimby and Lauriston S. Taylor.

Final Adjournment

BULLETIN OF THE INTER-SOCIETY COMMITTEE FOR RADIOLOGY

The following letter written by Dr. Thomas A. Groover* to the secretary of the Inter-Society Committee for Radiology is of such universal interest that Dr. Groover's permission to publish it has been secured.

The views of other readers on the topic of hospital relationships will be welcome. The members of the Inter-Society Committee would appreciate receiving comments from members who feel they have something to add to a consideration of the problem. The letter follows:

My dear Cahal:

Many thanks for your letter of December 20th reminding me of a promise to you and Ed Chamberlain to set down some of the thoughts which I expressed at our recent conference in Atlanta regarding the Physician-Hospital relationship problem in which radiologists are particularly interested.

Before attempting to do so first let me say that I think you rightly assume it to be at least part of your function as Executive Secretary of the American College of Radiology to help interpret the specialty to the public and to groups of physicians organized along lines similar to the one you represent. You rightly also regard it as your responsibility to interpret to the medical profession the concepts of the man in the street. To discharge such obligations is a whale of a job. It is one that invites sniping from all sides and requires a superabundance of imperturbability to carry on with it. Probably all of us are opportunists in varying degree and for that reason the gospel of a practical idealism which you are presumed to preach makes yours a most discouraging task. Now, I am about to lay on your doorstep another idea to interpret.

It is chock full of dynamite but I believe it is

* It is with regret that we announce the death of Dr. Groover, which occurred on April 20, 1940.—Ed.

fundamental to a reasonable understanding of the Physician-Hospital problem.

I think that the problem itself has been in the making for some time but is only just beginning to assume a recognizable form. It is born of the rapid institutionalization of medicine in recent years which still continues at an unabated pace. It should be remembered that the hospital was originally an institution only for the indigent and was commonly an annex of the alms house and prison. Under such circumstances it was natural for the doctor to expect others to furnish the necessary shop, tools and assistants to enable him to function in the hospital, particularly in view of the fact that his own indispensable service was rendered gratuitously. In those days those who were economically competent never thought of patronizing the hospital as patients. Later on when their prejudice against doing so was broken down and they began to patronize hospitals as patients, the hospitals continued to furnish the doctor, without charge to him, a shop in which to work; the tools of his trade; and a corps of professional and technical assistants. Prior to this time the doctor had furnished these items himself in caring for the economically competent. Obviously this circumstance places the doctor in a very vulnerable position with respect to his control of hospital policies. As hospitals continue to occupy an increasingly dominant position in the medical field, concurrently with an increasing institutionalization of medicine, the doctors' influence in controlling their policies may reasonably be expected to dwindle proportionately. As a corollary of the latter statement it is logical to conclude that the "fee for service" system of medical practice will decrease, and the "wage for service" system will increase. I think that this trend is now apparent in many departments of medicine—obviously so in radiology—and I believe that many adherents of the fee for service system in all departments of medicine will be drawn into the opposing group and still larger numbers will quite naturally grow up in it.

To state the problem in a somewhat different way I envision the hospitals as representing the capitalists of medicine, and would regard it as passing strange if they do not more and more adopt the capitalistic technique. By the latter I mean more particularly that increasing pressure will be exerted to hire professional help just as they do nonprofessional. Certainly the present differential in the doctor's favor will in one way or another be wiped out.

Assuming now that a large segment of the medical profession recognizes and views adversely the trend I have tried to indicate, it may well be asked what, if anything, can they do to modify it. To such I would have them remember that it is their prerogative to operate their own shop. In other words they can form a competing capitalistic group. There is abundant evidence to indicate that this is not an altogether fantastic idea or impractical task. If undertaken seriously it may well have a far reaching and salutary effect both for the medical profession and the public.

In the above brief commentary on the Physician-Hospital problem I trust that you will particularly note that it is not tinged with partisanship or special pleading. I have purposely refrained from even mentioning many highly important issues and implications which the basic theme suggests, feeling that to do so might obscure rather than clarify the latter. I would be glad to discuss some of the former with you when the opportunity offers.

Sincerely yours,

(Signed) Thos. A. Groover

KENTUCKY RADIOLOGICAL SOCIETY

The Annual Meeting of the Kentucky Radiological Society was held at the Brown Hotel, Louisville, Kentucky on Sunday, April 21, 1940. The meeting convened at 11:20 A.M. with Dr. D. B. Harding, President, presiding. Following the business session luncheon was served. After the luncheon Dr. Howard P. Doub, of Detroit, Michigan, addressed the Society on the subject of "Childhood Tuberculosis." His presentation was illustrated by numerous lantern slides. Following Dr. Doub's address cases illustrated by lantern slides were reported by members of the Society and were discussed by those present. The meeting adjourned at 5:30 P.M.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

Roentgen Diagnosis of the Extremities and Spine. (Ann. Roentgenol., Vol. XVII.) By Albert B. Ferguson, M.D., Director of Roentgenology, New York Orthopaedic Hospital; Instructor in Orthopaedic Surgery, College of Physicians and Surgeons, Columbia University. Cloth. Price, $12.00. Pp. 435, with 513 illustrations. New York: Paul B. Hoeber, Inc., 1939.

This latest addition to the Annals of Roentgenology presents the subject of skeletal roentgenology in the precise, organized fashion so characteristic of this author's teaching methods. The book is addressed to the medical profession at large and therefore attempts to justify the roentgenologic manifestations of skeletal disease on the basis of purely objective evidence which can be appreciated and understood by any careful observer.

No attempt has been made to treat separate disease entities exhaustively from all points of view; instead the text deals in an extremely orderly fashion with various appearances of bone and cartilage in health and disease. The introduction sets the pace of the entire volume by introducing the highly definitive roentgenologic nomenclature developed and employed by the author which is rigidly followed throughout the text. The reader may find in this lexicon of terms many which are not in common and widely accepted usage. He may disagree with the author's belief that neoplasia, lues, and nonspecific inflammatory disease, for example, produce individually characteristic degrees of bone density which can be recognized as such by the roentgenologist with any considerable degree of accuracy. It must be admitted, however, that the specific terminology employed is preferable to haphazard, wordy description. Never are descriptive terms used loosely or ambiguously; definitions provided at the outset are never violated.

This book is not one to be read lightly, for both in the matter of content and arrangement it requires the full and undivided attention of the reader. The specialized roentgenographic nomenclature mentioned above appears, wherever it occurs, in bold face type to arrest one's attention. Illustrative material is so profuse that repeated interruptions of continuity in the text are unavoidable, and clinical information about each case whose roentgenograms have been reproduced is cataloged at the end of each chapter and rendered accessible by means of reference numerals. These numerous annotations prevent brisk, casual reading.

Both the author and the publisher are to be complimented on the general excellence of this book. Because so many illustrations have been employed, it has obviously been necessary to limit the size of individual cuts which renders it somewhat difficult to quickly recognize the exact location of bones illustrated. For those who prefer to observe roentgenograms in the form of original negatives, these printed positives require mental transposition. Here again, however, uniformity and consistency have been the rule and in general the reproductions are of excellent quality. Virtually every phase of skeletal roentgenology has been richly and advantageously illustrated. Practitioners and students alike will find in Ferguson's contribution an excellent reference work.

Fred Jenner Hodges

Cancer Handbook of the Tumor Clinic, Stanford University School of Medicine. Edited by Eric Liljencrantz, M.D., Chief of Tumor Clinic, Stanford University School of Medicine; Consultant in Neoplastic Disease, United States Naval Hospital, Mare Island, and United States Marine Hospital, San Francisco. Cloth. Price, $3.00. Pp. 114, with 50 illustrations. Stanford University, California: Stanford University Press, 1939.

This book is a revision of the syllabus on the diagnosis and treatment of malignant tumors originally published at the Stanford University School of Medicine in 1937. It presents the methods of diagnosis and treatment of malignant neoplasms currently in use in the Tumor Clinic of that institution. The first twenty-four pages deal with general considerations, and here the up-to-date character of its summaries is evidenced by the inclusion of extra-chromosomal factors among the intrinsic causes of cancer, by brief discussion of the more im-

portant chemical carcinogens and by reference to the new-growths known to be induced by viruses. It is stated emphatically that whatever the theoretical dangers of biopsy may be, far more serious are the dangers of attempting radical treatment or of declaring the prognosis hopeless without tissue proof. Properly performed biopsy is less dangerous than is rough handling or massage by patient or physician. The principles of radiation therapy receive proportionally fuller exposition than do the other topics in this section and the Amstutz diagram illustrating the range and relationship of electromagnetic waves is reproduced. Chapters on cancer of the skin, eye and lip, oropharynx and neck, gastrointestinal tract, lung, breast, female generative tract, genitourinary tract, on leukemias and lymphoblastomas, on tumors of the central nervous system and on bone tumors follow. A bibliography with selected references arranged by chapter headings and a complete index are provided. For each common form of malignant disease there is a brief discussion of methods of diagnosis and of treatment. Naturally enough, not every reader will be in full accord with all of the methods of treatment advised, for there is still considerable diversity of opinion among competent authorities. Yet the methods given are those which have proved to be most useful in a cancer clinic in which the combined judgment of a group of specialists is utilized. As such, these recommendations must receive thoughtful consideration. Moreover, they represent very fully the prevailing methods in other active cancer clinics. This book will prove very useful to the postgraduate student in the field of neoplasia and to the general practitioner. Upon the latter it places the chief responsibility for the fate of the cancerous patient.

C. V. Weller

Tumors of the Skin, Benign and Malignant. By Joseph Jordan Eller, M.D., Attending Dermatologist, City Hospital, New York City; Consulting Dermatologist, French Hospital and Broad Street Hospital, New York City; Unity Hospital, Brooklyn; Morristown Memorial Hospital, Monmouth Memorial Hospital, Norwalk General Hospital, etc. Cloth. Price, $10.00. Pp. 607, with 401 illustrations. Philadelphia: Lea & Febiger, 1939.

Concise descriptions of the many tumors found in the skin illustrated with many good photographs and photomicrographs are presented in this volume. Histological studies of the relatively unimportant benign tumors included in the first section of the book are particularly valuable because they are not found in most texts. In a chapter entitled, "Nevi and Other Developmental Disturbances of the Skin," an attempt is made to unscramble a large group of poorly understood conditions known by a variety of names which are rather mystifying to the uninitiated.

A discussion of the etiology of tumors seems rather inadequate since no mention is made of the voluminous work recently published dealing with the carcinogenic properties of coal-tar derivatives and estrogenic substances.

Precancerous lesions are described in some detail and 250 pages are devoted to malignant new growths, including malignant melanomas, sarcomas, lymphomas and carcinomas peculiar to the epithelium covering the various portions of the body and its orifices. The author should be highly commended for the chapter on therapy because, so far as the reviewer is aware, he is the first American dermatologist to boldly advocate adequate doses of radiation for cancer of the skin since Pusey published his original book about thirty years ago. The treatment of a number of actual cases is illustrated with charts and in most instances efficient plans for treating the lesions with roentgen rays, radium, coagulation, or surgery are outlined. The proper use of only one method is advocated in each instance, rather than the old dermatological practice of combining several procedures in a half-hearted manner.

Although the care of small carcinomas is well covered, a section dealing with the use of high voltage roentgen rays and interstitial radium sources in the treatment of large carcinomas and metastatic lymph nodes should be added to the next edition. A statistical study of the results obtained with different methods in the author's large material would also be of great interest.

For the sake of completeness a chapter on the simple principles of cutaneous surgery and plastic repair is included and a short appendix contains practical and reliable data on radiation physics and dosage. The bibliography is ample, and the cooperation of a series of outstanding pathologists, surgeons, radiologists and dermatologists accounts for the unusual comprehensiveness of this very excellent book.

Charles L. Martin

THE COMPARATIVE VALUES OF CHEST ROENTGENOGRAMS MADE ON FILM AND ON PAPER FOR INDUSTRIAL SURVEYS. By Air Hygiene Foundation of America, Inc. Medical Series, Bulletin No. 11. Paper. Price, $2.00. Pp. 20, with charts and illustrations. Pittsburgh, Pa., 1939.

In 1938, the Air Hygiene Foundation requested the University of Pennsylvania to make a study of available roentgenologic methods for examination of the chest of large groups of employees with special reference to the primary importance of diagnostic accuracy, of time consumed in such examinations and cost involved in the equipment and photographic medium used. The study was directed by Dr. E. P. Pendergrass of the Department of Radiology of the Hospital of the University of Pennsylvania and technical aspects were developed by the staff of the Moore School X-ray Laboratory comprising Professor Charles Weyl, Dr. S. Reid Warren, Jr., and Mr. Dallett B. O'Neill. Forty-nine roentgenologists examined test roentgenograms and recorded their opinions in special questionnaires.

Two methods of examination were studied from the standpoints mentioned above: (1) the use of 14×17 inch roentgen film, and (2) the use of sensitized paper. The object of the study was to attempt to answer the question, "What are the comparative values of single roentgenograms on film and paper?"

The report consists of twenty pages and six large charts with several additional tables within the text. The material is divided into the following sections:

(1) The physical characteristics of roentgenograms on film and paper. (2) Preliminary experimental procedures. (3) Roentgenographic exposure techniques. (4) Test roentgenograms and questionnaires. (5) Physical data of test roentgenograms. (6) Roentgenologists' comments on test roentgenograms. (7) Conclusions.

Condenser discharge apparatus was used for both film and paper exposures. Comments of the roentgenologists who examined the roentgenograms are given in considerable detail and the description of the preliminary experimental procedures and techniques employed indicates painstaking effort to arrive at correct conclusions.

The authors conclude that their results demonstrate two points:

1. The paper roentgenograms produced in the tests were of better quality than those produced by other methods heretofore used in survey work.

2. Many roentgenologists learn easily and quickly the technique of viewing paper roentgenograms even though they may formerly have been unfamiliar with the use of this roentgenographic medium.

They admit that some time will be required to set up methods whereby paper roentgenograms may be routinely made in accordance with the technical procedures described in their report. They believe, however, that it is possible to devise and put into effect such technical methods ultimately as routine procedures. In view of the fact that no evidence was produced in their study to show that paper roentgenograms are in any way superior to those on film from the diagnostic standpoint, they feel it is best in the long run to devise a method of making roentgenograms on film quickly and at low cost. If a large group of employees is to be examined and a part of the examination is a single roentgenogram of each employee, then it is less expensive and less time-consuming to use paper in rolls than to use single pieces of film. Such a survey may be made with paper if the technical methods outlined in their report are used or if other methods are used which produce equal or better results.

This report is well worth careful consideration by all roentgenologists. For those whose practice includes surveys of industrial plants, schools, colleges, etc., it is an indispensable addition to their book shelves.

R. S. BROMER

A TEXTBOOK OF SURGERY. By John Homans, M.D., Clinical Professor of Surgery. Compiled from lectures and other writings of members of the Surgical Department of the Harvard Medical School. Fifth Edition. Cloth. Price, $8.00. Pp. 1272, with 530 illustrations. Springfield, Illinois: Charles C Thomas, 1940.

The fifth edition of this popular textbook of surgery has been extensively revised, if that is the term, with the complete replacement of outworn observations and procedures by the newer discoveries and advances in surgery. Every section of the book has been subjected to this process and there is included now in this edition the surgical advances that have occurred since the printing of the fourth edition. The pagination has remained unchanged and con-

sequently the book remains the same size, the new sections having replaced outworn items. It is in essence a rewriting of the work so that it retains its freshness and the charming personal style of the author. This edition, like the others, is an excellent example of the printer's and book-binder's art and it can be highly recommended to the student of surgery, especially to the one in medical school, as the book is after all written for him, and still continues to fulfill this function admirably.

FREDERICK A. COLLER

BOOKS RECEIVED

A TEXT-BOOK OF X-RAY DIAGNOSIS. By British Authors. In three volumes. Volume III. Edited by S. Cochrane Shanks, M.D., M.R.C.P., F.F.R., Honorary Director, X-Ray Diagnostic Department, University College Hospital; Radiologist, the Prince of Wales's General Hospital, etc., Peter Kerley, M.D., M.R.C.P., F.F.R., D.M.R.E., Physician to the X-Ray Department, Westminster Hospital; Radiologist, Royal Chest Hospital, etc., and E. W. Twining, M.R.C.S., M.R.C.P., F.F.R., D.M.R.E., Radiologist, Royal Infirmary, Manchester; Radiologist, Christie Hospital; Later Hunterian Professor, Royal College of Surgeons; Lecturer in Radiology, University of Manchester, etc. Cloth. Price, £3.3.0. Pp. 800, with 710 illustrations. London: H. K. Lewis & Co., Ltd., 1939.

THE 1939 YEAR BOOK OF RADIOLOGY. Diagnosis: Edited by Charles A. Waters, M.D., Associate in Roentgenology, Johns Hopkins University; Assistant Visiting Roentgenologist, Johns Hopkins Hospital, and Whitmer B. Firor, M.D., Associate Editor, Assistant in Roentgenology, Johns Hopkins University; Assistant in Roentgenology, Johns Hopkins Hospital. Therapeutics: Edited by Ira I. Kaplan, B.Sc., M.D., Director, Division of Cancer, Department of Hospitals, City of New York; Clinical Professor of Surgery, New York University Medical College; Director, Radiation Therapy Department, Bellevue Hospital, New York City, etc. Cloth. Price, $4.50. Pp. 528, with 509 illustrations. Chicago: The Year Book Publishers, Inc., 1939.

THE HOSPITAL CARE OF NEUROSURGICAL PATIENTS. By Wallace B. Hamby, M.D., F.A.C.S., Associate Professor of Neurology and Instructor in Surgery (Neurological Surgery), University of Buffalo School of Medicine, Buffalo. Cloth. Price, $2.00. Pp. 118. Springfield, Illinois: Charles C Thomas, 1940.

THE HYPOTHALAMUS AND CENTRAL LEVELS OF AUTONOMIC FUNCTION. Proceedings of the Association December 20 and 21, 1939, New York. (Research Publications, Association for Research in Nervous and Mental Disease, Vol. XX.) Editorial Board: John F. Fulton, M.D., Chairman, S. Walter Ranson, M.D., and Angus M. Frantz, M.D. Cloth. Price, $10.00. Pp. 980, with 319 illustrations and 35 tables. Baltimore: Williams & Wilkins Co., 1940.

L'ÉLECTRO ENCÉPHALOGRAMME: NORMAL ET PATHOLOGIQUE. Par Ivan Bertrand, Directeur à l'Ecole des Hautes Etudes, Jean Delay, Médecin des Hôpitaux de Paris, and Jacqueline Guillain, Assistante à l'Institut de Neurobiologie. Paper. Price, 94 fr. Pp. 294, with 94 illustrations. Paris: Masson et Cie, 1939.

TRAUMI CRANICI: CHIRURGIA—NEUROLOGIA—RADIOLOGIA. By Mario Lapidari, Ludovico Mucchi, and Virginio Porta. Con un capitolo sulla lesioni auricolari da trauma cranico di F. Carnevale Ricci. Prefazione de Mario Donati. Paper. Price, 50 lire. Pp. 430, with 101 illustrations. Belluno: Edizioni Casa Editrice Libraria Antonio Salvador, 1938.

ELECTROCARDIOGRAPHIC PATTERNS: THEIR DIAGNOSTIC AND CLINICAL SIGNIFICANCE. By Arlie R. Barnes, M.D., Mayo Clinic, Rochester, Minnesota. Cloth. Price, $5.00. Pp. 197, with 95 illustrations. Springfield, Illinois: Charles C Thomas, 1940.

PERIPHERAL VASCULAR DISEASES: DIAGNOSIS AND TREATMENT. By William S. Collens, B.S., M.D., Metabolist, Chief of the Clinic for Peripheral Vascular Disease, Chief of the Diabetic Clinic, Israel Zion Hospital, Brooklyn, etc., and Nathan D. Wilensky, M.D., Assistant in Clinic for Peripheral Vascular Disease, Assistant in Diabetic Clinic, Israel Zion Hospital, etc. Cloth. Price, $4.50. Pp. 243, with 77 illustrations. Springfield, Illinois: Charles C Thomas, 1939.

THE ELECTROCARDIOGRAM AND X-RAY CONFIGURATION OF THE HEART. By Arthur M. Master, B. S., M.D., F.A.C.P., Associate in

Medicine and Chief, Cardiographic Laboratory, the Mt. Sinai Hospital, New York; Associate in Medicine, the College of Physicians and Surgeons, Columbia University, New York. Cloth. Price, $6.50. Pp. 222, with 71 illustrations. Philadelphia: Lea & Febiger, 1939.

The Diagnosis and Treatment of Diseases of the Esophagus. By Porter P. Vinson, B.S., M.A., M.D., D.Sc., F.A.C.P., Professor of Bronchoscopy, Esophagoscopy, and Gastroscopy, Medical College of Virginia, Richmond, Virginia. Cloth. Price, $4.00. Pp. 224, with 98 illustrations. Springfield, Illinois: Charles C Thomas, 1940.

The Introduction of Gastro-enterology. Third Edition of The Mechanics of the Digestive Tract. By Walter C. Alvarez, Professor of Medicine, University of Minnesota, The Mayo Foundation, and a Senior Consultant in the Division of Medicine, The Mayo Clinic. Cloth. Price, $10.00. Pp. 778, with 186 illustrations. New York: Paul B. Hoeber, Inc., 1940.

Proctoscopic Examination and Diagnosis and Treatment of Diarrheas. By M. H. Streicher, M.S., M.D., Assistant Professor of Medicine, University of Illinois, College of Medicine, Research and Educational Hospital, and Department of Surgery, Grant Hospital of Chicago. Cloth. Price, $3.00. Pp. 139, with 39 illustrations. Springfield, Illinois: Charles C Thomas, 1940.

Orthopedic Operations: Indications, Technique and End Results. By Arthur Steindler, M.D., F.A.C.S., Professor of Orthopedic Surgery, The State University of Iowa, Iowa City, Iowa. Cloth. Price, $9.00. Pp. 766, with 322 illustrations. Springfield, Illinois: Charles C Thomas, 1940.

Endocrine Gynecology. By E. C. Hamblen, B.S., M.D., F.A.C.S., Associate Professor of Obstetrics and Gynecology, Duke University School of Medicine; Gynecologist in charge of the Endocrine Division and Sex-Endocrine Clinic, Duke University Hospital. Durham, North Carolina. Foreword by J. B. Collip, M.D., Gilman Cheney Professor of Biochemistry and Pathological Chemistry, McGill University, Montreal. Cloth. Price, $5.50. Pp. 453, with 169 illustrations. Springfield, Illinois: Charles C Thomas, 1939.

Handbook of the Hospital Corps, United States Navy, 1939. Published by the Bureau of Medicine and Surgery, under the Authority of the Secretary of the Navy. Cloth. Price, $1.75. Pp. 1015, with 201 illustrations. Washington, D. C.: U. S. Government Printing Office, 1939.

Ergebnisse der gesamten Tuberkuloseforschung. Band IX. Herausgegeben von H. Assmann, Königsberg I. Pr.; H. Beitzke, Graz; and H. Braeuning, Hohenkrug-Stettin. Paper, Price, RM. 56; bound, RM. 58. Pp. 577, with 135 illustrations. Leipzig: Georg Thieme, 1939.

Das Wesen und der Wert der Tomographie (Praktische Tuberkulose-Bücherei, Heft 23.) Von Dr. W. Deutschmann, Aus den Heilstätten der L.V.A. Berlin, Ärztlicher Direktor: Dr. Kremer. Paper. Price, RM. 3. Pp. 40, with 39 illustrations. Leipzig: Georg Thieme, 1939.

Grundlagen der Röntgendiagnostik und Röntgentherapie. Von Chefarzt Dr. G. Schulte, Knappschafts-Krankenhaus Recklinghausen, und Doz. Dr. med. habil. F. Kuhlmann, Medizinische Universitätsklinik Halle a. S. Paper, price, RM. 7.50; bound, RM. 8.50. Pp. 140, with 148 illustrations. Leipzig: Georg Thieme, 1939.

Ergebnisse der physikalisch-diätetischen Therapie. Ingemeinschaft mit Prof. Dr. W. Heupke, Oberarzt an der Med. Universitäts-Poliklinik Frankfurt a. M., Hofrat Dr. J. Kowarschik, Primärarzt und Vorstand des Institutes für physikalische Heilmethoden im Krankenhaus der Stadt Wien, and Doz. Dr. J. Kühnau, Direktor des Städt. Forsch.-Inst. für Bäderkunde und Rheumaheilanst Wiesbaden. Herausgegeben von Prof. Dr. H. Lampert, Direktor des Univ.-Inst. für physikalische Therapie, Frankfurt a. M., und des Univ.-Inst. für Quellenforsch und Bäderlehre, Chefarzt am Kreiskrankenhaus Bad Homburg v.d.H. Band 1. Paper, price, RM. 25.50; bound, RM. 27. Pp. 410, with 94 illustrations. Dresden and Leipzig: Theodor Steinkopff, 1939.

Handschrift und Eigenart der Krebsgefährdeten: Ein Beitrag zur Dispositionsforschung. By Etel Vértesi. Cloth. Price, $4.00. Pp. 297, with 130 illustrations of handwriting. Budapest: Brüder Tisza, 1939.

DEPARTMENT OF TECHNIQUE

Department Editor: ROBERT B. TAFT, M.D., B.S., M.A., 105 Rutledge Ave., Charleston, S. C.

A METHOD FOR THE PREPARATION OF RADON OINTMENT

By LESTER J. PERLMAN
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IN A RECENTLY published paper Uhlmann has again called attention to the value of radon ointment in the treatment of irradiation injuries. Eidinow has described its use in other skin conditions. Radon ointment is a physical mixture or solution of a minute quantity of gaseous radon in vaseline. A short time after its preparation, this mixture also contains small but important equilibrium quantities of the radioactive decay products of radon. The method given below was devised for the routine preparation of such a radon ointment.

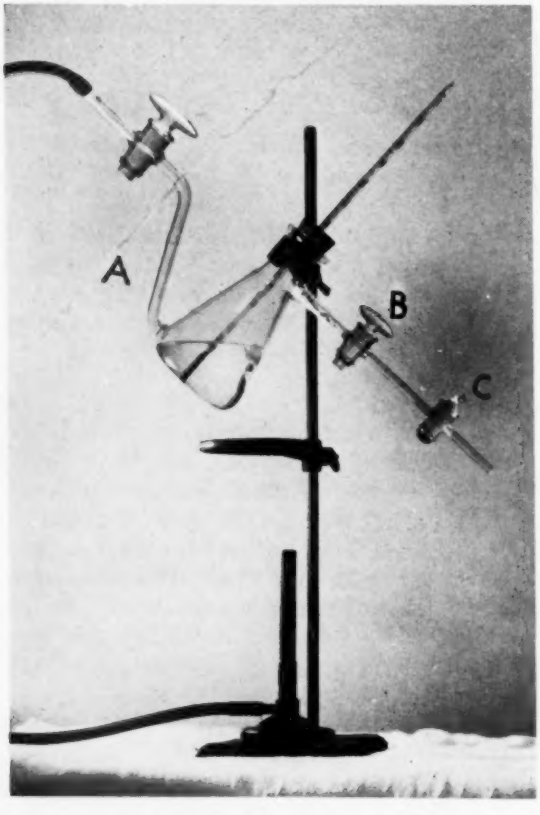

FIG. 1. The apparatus tilted for evacuation; the water bath is removed to show the vaseline level.

The radon used is the "residual fraction" obtained in the preparation of radon implants after the method of Failla and Duane. It is contained at $\frac{1}{3}$ to $\frac{1}{2}$ atmospheric pressure in glass capillary tubes less than 1 mm. in diameter and 20 to 50 mm. long.

The apparatus used is shown in Figure 1 and is constructed of an ordinary heavy-walled "Pyrex" filter flask with an additional sidearm (*A*) sealed at the bottom angle of the flask and curving upward. The upper sidearm (*B-C*) bears in series two "Pyrex" stopcocks (*B*) and (*C*) of 2 mm. bore, while the other sidearm (*A*) carries one stopcock (*A*) of 4 mm. bore. Two sets of apparatus are used, one of 125 cc. capacity for the preparation of 2 oz. (60 cc.) of ointment, and one of 250 cc. capacity, for the preparation of 4 oz. of ointment. In use the flask is supported in a hot water bath (not shown in the figure) on a ring-stand by means of a burette clamp having a universal joint.

With stopcocks (*B*) and (*C*) in the open position the radon tube is placed in sidearm (*B-C*) and with a thin applicator stick is moved into position within the bore of stopcock (*B*). A trace of stopcock grease serves to maintain this position during subsequent manipulation of the apparatus. Stopcock (*C*) is then closed.

The vaseline, melted in its original con-

tainer in the water bath, is poured into the flask, and the flask is sealed with a one-holed rubber stopper bearing a thermometer. The apparatus is then tilted until sidearm (*A*) is brought above the level of the liquid vaseline, and the flask is lowered into the water bath, leaving the stopcocks above the water. A rubber tube from a vacuum pump is connected to the sidearm (*A*), and, with the water bath at close to boiling, the flask is slowly evacuated through stopcock (*A*), until the frothing of the vaseline is in large measure ended. The vacuum so obtained later facilitates the rapid diffusion of the radon through the apparatus. Stopcock (*A*) is closed, the rubber tubing removed, and the flask returned to upright position in the water bath.

Now stopcock (*B*) is turned through 180°, breaking the radon tube and permitting the radon to diffuse into the flask. The burner is removed from under the water bath, and the burette clamp is disconnected from the ringstand. A rotary motion of the flask, still in the water bath, imparts a swirling agitation to the vaseline, speeding the dissolving of the radon. The whole is permitted to cool slowly with intermittent agitation for about twenty minutes, until the thermometer reads 50–55° C. (The vaseline will not flow readily below about 50° C.)

Stopcock (*C*) is gently opened, admitting air to the flask, the apparatus is removed from the water bath, and the vaseline is poured through sidearm (*A*) into a screw-capped jar which is immediately capped tightly. Care must be taken to close stopcocks (*A*) and (*C*) before all the vaseline has drained from sidearm (*A*). This traps most of the undissolved radon in the flask.

Measurements with a gamma-ray electroscope indicate a yield of about 65 per cent of the original radon in the ointment. Measurements of unopened jars of ointment on successive days show a decrease of activity in accordance with the rate of decay of the radon (about half-destroyed every four days) and give no evidence of loss from closed jars by leakage or "evaporation." Thus the preparation and measurement of the ointment some days before use is feasible.

The method gives consistent results over a wide range of radon concentrations. It has also been applied to the preparation of beeswax beta-ray plaques of low intensity such as those used in dermatology by Lomholt, and its use may be extended to the preparation of radon solutions in other media. The yield may be expected to vary with the solvent and with the temperature at which the process is completed.

This method is alternative to other methods for the production of radioactive vaseline which have been published. References to some of these methods are given.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

ABDOMEN

Chamberlin, George W. The roentgen anatomy of the small intestine. *J. Am. M. Ass.*, Oct. 21, 1939, *113*, 1537–1541.

Roentgenologically, the small intestine is a highly active and dynamic organ with certain characteristic anatomic and physiologic features. The meal that the author has used is made of 5 ounces of distilled water and 5 ounces of barium sulfate. Water is distilled to remove the chlorine, which may produce a disturbance in the roentgen appearance of the intestinal tract. In normal controls, the head of the meal reaches the cecum in from one and a half to three hours. The small intestine is completely empty in from five to six hours. The mucosal pattern of the small intestine shows many variations which seem to be specific for a given set of physical conditions. Such a pattern is derived from the primary circular folds of Kerkring and from the secondary induced folds which may occur in the mucous membrane. The pattern of a given segment depends on its anatomic character and also on its physiologic activity at the time of the examination. Intra-abdominal hernia can be diagnosed by roentgen study of the small intestine. In this condition the coils are grouped closely and they may occupy the right, left or midabdominal position. Congenital diverticula of the small intestine occur most frequently in the duodenum. Congenital membranes and veils attached to the duodenum may produce roentgenologic appearances which cannot be differentiated from pericholecystic adhesions or duodenal ulcers. Congenital defects which result in a narrowed small intestinal lumen or complete atresia are most commonly found in children. In most of the cases, these defects are incompatible with life. Meckel's diverticulum may sometimes be found. Whenever delayed motility occurs in the ileum, one should examine the intestine carefully for this anomaly. Ileal stasis may result from a Lane's kink. One may suspect this condition if a partial obstruction is associated with a kinked and somewhat fixed terminal ileum.—*S. G. Henderson.*

Weber, Harry M. Roentgenologic manifestations of non-neoplastic lesions of the small intestine. *J. Am. M. Ass.*, Oct. 21, 1939, *113*, 1541–1546.

Peptic ulcer of the duodenum and of the jejunum occurring after gastroenterostomy is omitted. Acute inflammatory processes of the small intestine are not included because patients afflicted with them rarely are, and probably never should be, submitted to roentgenologic examination. Syphilitic and actinomycotic lesions of the small intestine are exceedingly rare. The technique used in examining the small intestine is described.

Tuberculous enteritis and a nonspecific form of chronic enteritis of undetermined origin are the most common types of chronic enteritis encountered in practice. The two diseases have many clinical, morphologic and roentgenologic features in common. Usually in tuberculous enteritis a combination of ulceration and hyperplasia is observed. As a rule, tuberculous lesions are distributed throughout the colon and in the small intestine as well, and especially in the ileocecal region, but there are many exceptions. In 1932 Crohn, Ginzburg and Oppenheimer reported a series of cases of benign, subacute or chronic, necrotizing and cicatrizing inflammation of the small intestine. Macroscopically, it is always difficult, and usually impossible, to distinguish the non-tuberculous from the tuberculous form. Close comparison of the roentgenologic appearances often shows a different roentgenologic "look" of the two diseases. The contours of the tuberculous intestine have typically a rougher, more corrugated appearance corresponding to a more irregular, disconnected insemination of the ulcerohyperplastic process. In the non-tuberculous form of chronic enteritis the contours are characteristically smooth and the narrowing is uniform, corresponding to the typical diffuse, even development of the underlying pathologic process. Other aids in the differentiation are chiefly those concerned with the exclusion of tuberculosis.

Peculiar changes in the roentgenologic appearance of the small intestine are often observed in certain states of dietary deficiency, especially when steatorrhea, with or without

diarrhea, is one of the principal clinical features. One of the surprising features is the marked depression of motility throughout the intestinal tract. Peculiar segmentation of the intestinal loops is commonly found. Contracted segments are observed to alternate irregularly with dilated ones. The contours of well distended segments may be abnormally smooth at one period of roentgenoscopic observation, abnormally shaggy at another. Fantastic agglomerations of the opaque suspension take place. The author believes that the roentgenologic changes are plausibly explained by holding the degenerative changes accountable for the abnormal motility and for some of the bizarre intestinal patterns observed, while abnormal secretions are made responsible for the other peculiar roentgenologic manifestations.

Diverticula are found in the duodenum more frequently than in any other part of the intestine except the sigmoid colon. The most common site of origin is near the ampulla of Vater. The diverticula found in the jejunum are larger, as a rule, than those in the duodenum, and they are more frequently multiple than single. Diverticula are but rarely found in the ileum, and those not designated as Meckel's diverticula rarely are associated with clinical symptoms. Meckel's diverticulum occurs in about 2 per cent of the population, males predominating in a ratio of 2:1. It is always found somewhere in the first 5 feet (150 cm.) of ileum above the ileocecal valve. Only 8 of 20 patients reviewed by Pemberton and Stalker had symptoms believed to be due to the diverticulum. Up to the present time Meckel's diverticula have been demonstrated roentgenologically on but 6 occasions at the Mayo Clinic. Meckel's diverticulum will usually be found in those coils of the lower part of the ileum that are situated near and somewhat to the right of the midline and at or near the level of the umbilicus.

Of the extra-enteral non-neoplastic processes which extend to and involve the small intestine, perforating diverticulitis of the sigmoid colon and salpingo-oöphoritis seem to be encountered most frequently. If actual perforation into the intestinal lumen has not taken place, considerable deformity of the affected segment may be observed, yet as the mucosal surface is carefully examined it will be noted that the mucosal pattern, although altered considerably by functional changes and by edema and submucous infiltration, will be left unbroken throughout the deformed segment.—*S. G. Henderson.*

KIEFER, EVERETT D. Clinical aspects of chronic disorders of the small intestine. *J. Am. M. Ass.*, Oct. 21, 1939, *113*, 1546–1552.

There are few symptoms which are highly diagnostic of disease of the small intestine. The almost completely fluid nature of the content of the small intestine makes for an "all or none" type of obstruction. Abdominal distress immediately after meals, flatulence and diarrhea are suggestive of hypermotility. Grossly inadequate absorption results in large, foul, fatty stools, failing nutrition, calcium imbalance and avitaminosis.

The general physical signs of disease of the small intestine are malnutrition, anemia and signs of vitamin deficiency. An important abdominal finding may be a mass.

By far the most important single laboratory procedure is the roentgen examination of the gastrointestinal tract, but lesions of the small intestine are not found unless they are looked for. A film taken between two and three hours after the barium meal has much more diagnostic value than the ordinary six hour film.

One of the commonest forms of chronic organic disorders of the small intestine is the intermittent obstruction caused by postoperative adhesions. Characteristically the physical examination and the gastrointestinal roentgen films may be entirely negative during the intervals between attacks. Due to fear of eating because of the resulting pain, frequent vomiting and diarrhea, mild states of malnutrition and vitamin deficiency are common, and occasionally avitaminosis develops comparable to severe pellagra.

An annular carcinoma of the small intestine characteristically tends to give rise to slowly progressive obstruction with increasing pain, vomiting and loss of weight. New growths which are mural or polypoid in type are the most frequent cause of intussusception in the adult and are prone to cause intermittent attacks of obstruction. Meckel's diverticulum is another important cause of intussusception in young adults. In cases of bleeding from the lower portion of the intestine, particularly in children and young adults, Meckel's diverticulum should be considered, since the occurrence of aberrant gastric mucosa within the sac giving rise to peptic ulceration, hemorrhage and perforation is a well known clinical entity.

A subacute or chronic non-ulcerative inflammation of the small intestine is frequently seen.

From a roentgenologic point of view, chronic ulcerative enteritis of either the small or the large bowel produces obliteration of normal outlines, loss of flexibility, shortening of loops, stenosis and contraction of the lumen and occasional fistula formation. Tuberculous enterocolitis produces changes in the ileum and proximal colon which, from a roentgenologic standpoint, are indistinguishable from nonspecific enteritis. Hyperirritability of the intestine is indicative of early ulcerative lesions in the mucosa.

Avitaminosis may lead to secondary changes in the intestinal tract which are sufficiently definite to be demonstrated by roentgen study. Irregular distortions of the normal mucosal pattern, localized dilatation of the lumen and a tendency for the barium sulfate to form pockets in isolated loops are noted. Purely functional disorders of the small intestine are usually manifested by signs and symptoms of hypermotility.—*S. G. Henderson.*

Winters, William L., and Egan, Sherman. Incidence of hemorrhage occurring with perforation in peptic ulcer. *J. Am. M. Ass.*, Dec. 16, 1939, *113*, 2199–2204.

Authors' Summary and Conclusions. Three hundred and sixty-one patients with perforated peptic ulcer that entered Cook County Hospital during the years 1935–1938 inclusive were reviewed to note the incidence of hemorrhage. Bleeding and perforation in a peptic ulcer do occur together. For the four years reviewed, bleeding was present in 10 per cent of the patients with perforated ulcer, and bleeding and perforation occurred in approximately 1 per cent of all patients admitted with the diagnosis of peptic ulcer during the years 1937 and 1938. Approximately 60 cc. or more of blood has escaped into the bowel when a patient has melena. Perforation in peptic ulcers occurred more often in males than in females. It occurred most frequently in the fourth decade, although the fifth decade showed almost the same number of cases. Bleeding and perforation occurred most frequently together in the sixth decade. Hemorrhage that follows surgical repair of a perforation should arouse suspicion that an ulcer situated elsewhere in the gastrointestinal tract may be responsible for the bleeding.—*S. G. Henderson.*

Stone, Harvey B., and McLanahan, Samuel. Surgical aspects of carcinoma of the large bowel. *J. Am. M. Ass.*, Dec. 23, 1939, *113*, 2282–2288.

In the presence of demonstrable visceral or peritoneal metastases it is often justifiable, and indeed good judgment, to remove an operable obstructing lesion. In a number of cases before ascertaining the operability of a given tumor it is necessary to make a careful, discreet beginning of resection. For the inoperable low sigmoid or rectal growth which at the time of exploration is not obstructing, a knuckle of sigmoid proximal to the growth is brought out through a short left McBurney incision and sutured to the skin. The second stage can be performed when necessity dictates, or may never need to be done at all. In the presence of an inoperable tumor and more especially in the presence of a recurrence, irradiation is often helpful.

Two complications, acute obstruction and perforation, may require prompt operation and may so obscure the diagnosis as to make it clear only when exploration has been carried out. Partial intestinal obstruction represents the major problem to be solved before the patient is fit for the removal of his growth. The authors believe that in the majority of cases the bowel can be safely and satisfactorily decompressed and cleansed without recourse to any sort of enterostomy. Should it appear after a reasonable interval that these measures have been ineffective and that the patient continues to exhibit signs of partial obstruction, surgical drainage of a proximal segment should be carried out. Preliminary drainage of the bowel may also be called for with patients who are poor risks by reason of age or of associated diseases.

In selecting the type of procedure for lesions in the colon, the principle generally adhered to in this series of cases has been aseptic end to end anastomosis following an adequate resection of the growth and its adjacent mesentery. Seventy-one cases of aseptic anastomosis of the Parker-Kerr or clamp type yielded a mortality of 11.2 per cent, while 19 cases of open anastomosis yielded a mortality of 26.3 per cent. Concomitant decompression in the absence of preliminary drainage should be used more frequently. In the management of the solitary, sessile polyp of the rectum having malignant characteristics with no gross or microscopic invasion of the muscularis mucosae, early local excision is performed. The patient is then carefully observed and, if there is evidence of recurrence of the polyp, excision is again performed. In attacking rectal cancer, radical removal of lymphatic structures must not be compromised.

The preference throughout this series has been for one stage abdominoperineal resection. Either during or immediately following a resection of the large bowel, the patient should receive as a routine procedure a transfusion of blood. Other intravenous fluids should be given in large enough amounts to insure an adequate urinary output.

Among 166 resections there were 23 deaths, or a mortality rate of 13.8 per cent. While only 56 per cent of the deaths are directly attributable to the operative procedure, the incidence of peritonitis is high enough to stress the importance of an aseptic type of anastomosis and the desirability for more frequent employment of concomitant bowel drainage.—*S. G. Henderson.*

Swinton, N. W., and Warren, Shields. Polyps of the colon and rectum and their relation to malignancy. *J. Am. M. Ass.*, Nov. 25, 1939, *113*, 1927–1933.

During the past ten years the treatment of carcinoma of the colon and rectum has been vastly improved. However, in reviewing a series of 300 patients with carcinoma of the colon and rectum, it was discouraging to find that the average duration of symptoms at the time of resection was nine months. This was the same duration that was revealed by a similar study five years previously.

In this paper the authors review a series of 156 patients with benign and malignant polyps of the colon and rectum who have been operated on at the Lahey Clinic during the past eight years. In this study the term polyp will include not only those pedunculated tumors arising from the wall of the large bowel but also those sessile tumors arising from mucous membrane which have no demonstrable pedicle. Clinically, mucosal polyps are classified as benign or malignant, single or multiple, and cases of multiple polyps are referred to as multiple polyposis. Histologically, the structure of polyps varies markedly. The covering epithelium ranges from the normal mucosa of the large intestine to irregular glands, variable in size and shape and lined with tall columnar epithelium with large, vesicular nuclei and prominent nucleoli frequently containing mitotic figures. The mucosa of the polyp always merges smoothly with that of the adjacent normal intestinal wall. The authors have found it possible to demonstrate histologically all stages in the sequence of change from normal colonic mucosa to actual adenocarcinoma.

The etiology of polyps of the colon and rectum has not been accurately established. McKenny obtained convincing evidence of the congenital nature of the cases of multiple polyposis of the entire colon. In the multiple polypoid-like structures which may develop in cases of ulcerative colitis the mucosa is never normal, nor is there the usual hyperplastic change seen in polyps. Following healing of the acute ulcerative process these pseudopolypoid tumors have been known to regress and disappear. The differentiation between ulcerative colitis in which polypoid changes have taken place in the mucous membrane and multiple polyposis associated with blood and increased amounts of mucus in the stool must be recognized. The majority of polyps of the large bowel are believed to be true tumors.

The location of the polyps found in this series is identical with the generally recognized distribution of carcinoma in the colon and rectum. Seventy per cent of the polyps were visualized through the 10 inch sigmoidoscope. The high incidence of multiple polypoid lesions, both benign and malignant, must be recognized and emphasized. In this series of 156 patients the polypoid lesions were multiple in 35 per cent, and in 121 cases malignant polyps were found. Polypoid disease may be found at any age and evenly distributed among males and females.

Polyps do not give rise to symptoms early in their development. As polyps become larger, the incidence of bleeding, mucus and rarely obstructive symptoms will be more frequent. Likewise the more extensive the involvement of the colon and rectum with polypoid disease, the greater the glandular development and the higher the incidence of bleeding and mucous discharges. In malignant polyps the symptomatology does not differ from that of the other types of malignant disease found in the large bowel. The importance of rectal bleeding, altered bowel function and the presence of unexplained abdominal pain in the early diagnosis of malignant disease is emphasized.

All patients with rectal and colon disorders should be examined by sigmoidoscope and by barium enema. The patient should be prepared for roentgen study by the use of castor oil and a cleansing enema. The use of the contrast air enema is helpful in localizing small organic lesions in the colon.

Microscopically, it is relatively difficult to determine the presence or absence of malignant change in intestinal polyps. Definite lymphatic

or intravascular invasion nearly always means a clinical malignant condition. Different portions of the polyp may present entirely different histologic pictures. The entire polyp together with its base must be examined microscopically for an accurate diagnosis of malignancy. The visualization and palpation of polypoid structures are of the utmost importance in establishing their benign or malignant nature. Fourteen per cent of the malignant tumors of the colon and rectum can histologically be demonstrated to have arisen in benign mucosal polyps. All polyps of the colon and rectum should be regarded as pre-malignant lesions.

Removal or destruction by fulguration of all polypoid structures in the colon and rectum is necessary if one is to detect early malignant change and prevent subsequent development of carcinoma in this region.—*S. G. Henderson.*

GENITOURINARY SYSTEM

Albright, Fuller, Sulkowitch, Hirsh W., and Chute, Richard. Nonsurgical aspects of the kidney stone problem. *J. Am. M. Ass.*, Dec. 2, 1939, *113*, 2049–2053.

The approach to this entire subject is based on the following major premise and its corollary:

Premise: A patient with urine of such composition that some crystalloid precipitates out of it is predisposed to the formation of a stone composed largely of the precipitated crystalloid (compare cystine stone in cystinuria, uric acid stone in gout and calcium phosphate or calcium oxalate stone in hyperparathyroidism).

Corollary: In a case in which there is a tendency for stones composed predominantly of a certain crystalloid to form, treatment should be directed to altering the composition of the urine in such a way that solution of the crystalloid is favored.

In addition to the foregoing propositions, stasis undoubtedly is a factor, while infection, although also a factor, probably plays its chief rôle by changing the composition of the urine.

There are four common types of kidney stones —calcium phosphate, calcium oxalate, uric acid and cystine. The urine should be made acid for calcium phosphate stones and alkaline for uric acid and cystine stones. With oxalate stones the pH of the urine is unimportant. Staghorn stones are nearly always composed of calcium phosphate or cystine. Very suggestive of cystine stones is the coalescence of several small stones to form a large one. The lamellar structure of phosphate stones is often discernible in the roentgenogram. Hyperparathyroidism usually causes calcium phosphate stones but occasionally calcium oxalate ones. A structure suggestive of a snowflake with spicules radiating from a central focus is pathognomonic of calcium oxalate. Failure of the stone to show in the roentgenogram is strong evidence in favor of a uric acid stone.

The dissolution of stones is not an impossibility. By keeping the urine alkaline, a cystine stone in the kidney pelvis may be caused to disappear. Attempts to dissolve calcium phosphate stones by keeping the urine acid have usually been largely unsuccessful. The stones may not become larger, but seldom get smaller. The reason for the poor results is that acid regimens increase the amounts of phosphate and calcium in the urine and thus tend to make it saturated. Attempts have been made to inject some "dissolving" substance by the retrograde method. In one case in which there were multiple stones (believed to be calcium phosphate) in the urinary bladder, dissolution of the stones was brought about by injecting a solution of sodium citrate—citric acid at a pH of 4.0. This solution combines the effect of acids in dissolving phosphates with a specific effect of citrate in dissolving calcium salts by decreasing the calcium ion concentration. It is possible that results may be obtainable in dissolving this type of stone even in the kidney pelvis. Recent incomplete studies suggest that sodium hexametaphosphate solutions may be even more effective than citrate solutions. This substance will actually dissolve calcium oxalate in a test tube.—*S. G. Henderson.*

SKELETAL SYSTEM

Spurling, R. Glen, and Bradford, F. Keith. Neurologic aspects of herniated nucleus pulposus at fourth and fifth lumbar interspaces. *J. Am. M. Ass.*, Dec 2, 1939, *113*, 2019–2022.

On the basis of the authors' experience with a series of 85 low intraspinal lesions treated surgically, they present what they have found to be the characteristic clinical picture of herniated nucleus pulposus at the fourth and fifth lumbar interspaces. Neoplasm along the course of the sciatic nerve, rectal or pelvic disease and disease of the osseous structures must be ruled out by regional and roentgenologic examinations.

The relations between the fifth lumbar nerve and the disc between the fourth and fifth lumbar vertebrae and between the first sacral nerve and the lumbosacral disc are especially important. The nerve roots forming the cauda equina are freely movable in the large lumbar canal except as they approach their exits, where they are fixed. Therefore displacement of the roots is possible, except near the port of exit, without neurologic deficit. The dural sleeve of the first sacral nerve separates from the thecal sac above the lumbosacral disc and can thus be compressed without deforming the sac. Recent studies indicate that there is a profuse supply of sensory nerve endings from the recurrent branches of the lumbar nerves in the annulus fibrosus and the posterior longitudinal ligament.

Symptoms. The occurrence of severe, persistent sciatic pain is of greatest importance diagnostically, especially if it is exaggerated by coughing, sneezing or straining. Points of greatest intensity are likely to be in the gluteal region, the posterior aspect of the thigh, the back of the knee or the lateral aspect of the leg or ankle. In almost every case incapacitating pain low in the back precedes the sciatic pain by weeks, months or years. The pain low in the back is variable or intermittent and is usually intensified by bending or lifting. Tingling, prickling, cold or numb sensations occurring below the knee in the lateral aspect of the leg or in the foot are characteristic of herniated nucleus pulposus at the fourth or fifth lumbar interspace.

Important clinical findings are a stiff lumbar spine, severe sciatic pain with a positive Lasègue sign, hypesthesia of the foot and lateral aspect of the leg and diminution or absence of the ankle jerk. Listing to one side is common. Limitation of flexion of the lumbar spine may be marked. Tests of the motor power are usually not of much aid because patients confuse pain on using the affected part with weakness. More important is diminution or absence of the ankle jerk, which usually occurs with herniation at the lumbosacral disc. The sensory changes are most important in making the diagnosis. Herniation at the fourth lumbar disc (involvement of the fifth lumbar and first sacral nerves) usually results in hypesthesia of the anterolateral aspect of the leg with inclusion of the great toe, while herniation at the lumbosacral disc (involvement of the first and second sacral nerves) gives hypesthesia of the posterolateral aspect of the leg with inclusion of the lateral aspect of the foot. Patients with herniation of the nucleus pulposus at the fourth lumbar and the lumbosacral disc have in common pain low in the back, severe sciatic pain, and hypesthesia or anesthesia below the knee. True sciatic pain is not caused by involvement of the ligamentous structures alone. If the nucleus pulposus extrudes through the annulus fibrosus without causing nerve compression the lesion remains in the category of purely ligamentous injury. The reliability of these neurologic symptoms and signs is attested by the fact that 9 consecutive herniations of the nucleus pulposus have been removed without confirmation with iodized oil or other contrast media.—*S. G. Henderson.*

Chamberlain, W. Edward, and Young, Barton R. The diagnosis of intervertebral disk protrusion by intraspinal injection of air; air myelography. *J. Am. M. Ass.*, Dec. 2, 1939, *113*, 2022–2024.

Gaseous contrast media have been used as a routine for the past three and one-half years with all patients who have had sufficient symptoms and neurologic evidence to cause suspicion of an intraspinal lesion. Oxygen is now used because it is absorbed faster than air and produces less discomfort. In an experience based on more than 300 spinograms, in each case in which operation was performed the exact level of the lesion determined by myelographic examination was verified by laminectomy.

The technique of injection varies somewhat, depending on the level of the lesion. The technique of and indications for injection at different levels are described. If a lesion is suspected below the third lumbar vertebra, with the head of the table lowered to an angle of from 20 to 25 degrees using an 18 or 20 gauge spinal needle inserted into the subarachnoid space at the second lumbar interspace, spinal fluid and air are exchanged in 5 cc. quantities until air escapes through the needle. In case the lesion is believed to be above the third lumbar vertebra, the spinal needle is inserted in the third lumbar interspace with the patient in a horizontal position and a Queckenstedt test is done. If this test shows a partial or complete block, from 3 to 6 cc. of spinal fluid is carefully replaced by an equal amount of air and the patient is examined in the sitting posture. If the Queckenstedt test is negative, the dorsal sac can be visualized by replacement of spinal fluid with air by either lumbar or cisternal puncture.

Visualization of air in the spinal canal depends on roentgenograms of good contrast and detail. "Overexposed" films give more information, so the kilovoltage is raised from 8 to 10 above that necessary for spinal detail. The minimal film requirements in the lumbar region are stereoscopic lateral and anteroposterior projections. In the upper dorsal or cervical region, it is advisable to take stereoscopic oblique projections as well as the lateral ones.

The diagnosis of a herniated disk depends in most cases on the indentation or encroachment of the limiting membrane of the subarachnoid space. The one exception to this is when the disk has produced a complete block of the canal. Here the inferior margin of the disk is easily demarcated by the air bubble trapped under it. The indentation of the air column due to a herniated disk is not always seen on the lateral projections. In a number of cases the defect was visualized only on the anteroposterior projections as a bilateral waist-like constriction or a unilateral marginal indentation. A major advantage of air and oxygen as contrast media for myelographic examination is the fact that their use does not entail leaving unabsorbable and possibly irritating substances in the spinal canal.—*S. G. Henderson.*

Camp, John D. The roentgenologic diagnosis of intraspinal protrusion of intervertebral disks by means of radiopaque oil. *J. Am. M. Ass.*, Dec. 2, 1939, *113*, 2024–2029.

Pathologic studies of protruded intervertebral disks indicate that the protruded fragments are composed of fibrocartilage, portions of the nucleus pulposus and occasionally remnants of the notochord. These structures are not ordinarily opaque to roentgen rays and for this reason the roentgenologist is dependent on the use of some contrast agent for the indirect visualization of the protrusion. Iodized oil, when employed under proper circumstances, has resulted in an accuracy of diagnosis that is shared by few other roentgenologic procedures. The chief objection to the use of iodized oil is that it is more or less of an irritant to the meninges and is contraindicated in the presence of inflammatory disease. The use of air or oxygen has much in its favor but there are certain decided disadvantages. Because of the difficulty in controlling the position and distribution of the air (or oxygen) its use with any satisfaction is restricted to the lumbar canal. The accuracy of the diagnosis with air is not equal to that attained with iodized oil.

No contrast agent should be used unless the clinical and neurologic examination indicates the possible presence of an intraspinal lesion that cannot be localized by ordinary clinical procedures. Because air or oxygen is very difficult to hold in position in the thoracic or cervical portion of the spinal canal, and because the superimposition of the shadow of air in the trachea, larynx and pharynx renders the interpretation of resulting shadows exceedingly difficult or impossible, iodized oil is the medium of choice for the demonstration of lesions at or above the conus. The great majority of protruded intervertebral disks occur in the lumbar and lumbosacral regions where they are accessible to examination by either air or iodized oil. If air studies are negative, inconclusive or unsatisfactory, and the history and neurologic examination are suggestive of the presence of a protruded disk, iodized oil should be used to check the spinogram. In the interest of early diagnosis and for the localization of lesions before obstruction has occurred, it is necessary to use a quantity of iodized oil sufficient to fill the subarachnoid space completely at any desired level. Five cubic centimeters of iodized oil is the optimal volume for accurate and consistent localization of non-obstructing lesions.

The lumbar injection of iodized oil is preferred because it is easier and safer to carry out than cisternal puncture and will facilitate the keeping of the oil together as one mass in the lower part of the spinal column. The iodized oil used should be clear, transparent and only faintly yellow. Prior to injection the ampule is warmed to a temperature of 105° F.

It is desirable that the roentgenologic study be carried out as soon after the injection as possible. Some method of quickly recording the fluoroscopic image on films is highly desirable. If the result of the examination of the lumbar spinal subarachnoid space is negative, it is important to examine the subarachnoid space higher up. Fifty per cent of patients with tumors of the spinal cord located in the thoracic region and 30 per cent of patients with such tumors located in the cervical region have low back or sciatic pain or both as an associated or coincident symptom.

Usually the protruded fragment is situated in the anterior portion of the spinal canal and will produce its maximal effect on the column of iodized oil when the patient is lying in a prone

or prone-oblique position. The classic defect is a sharply defined unilateral rounded indentation of the iodized oil shadow opposite an intervertebral disk. Midline protrusions when of moderate size may produce only a central defect. Except as the iodized oil deformity may be influenced by the presence of associated hypertrophy of the ligamentum flavum, the larger the protrusion the greater the obstruction of the subarachnoid space will be, and the greater the tendency to produce a bilateral deformity. Localized hypertrophy of the ligamentum flavum without coincident protrusion of a disk may imitate all the clinical phenomena of a protruded intervertebral disk and is characterized in the lateral view by a broad or rounded indentation on the posterior aspect of the column of iodized oil between contiguous laminae. In the prone or supine position the hypertrophy may be portrayed by broad indentation of the column of iodized oil, generally bilateral. When considerable hypertrophy of the ligamentum flavum accompanies a large protruded disk, the mass of iodized oil is compressed between the protruded disk anteriorly and the hypertrophied ligamentum flavum posteriorly and laterally. In about one-third of the cases of protruded intervertebral disk, lateral or posterior displacement of the nerve root shadows of the cauda equina or both will be visible at the site of the protrusion.

The significant symptoms of a protruded disk are the result of pressure exerted on the nerve roots by the protruded fragments. Edema of an affected nerve root may result in three ways: (1) by irritation of the root as it passes over the protruded disk, (2) by compression of the root between a protruded disk and the contiguous pedicle of the vertebra or (3) by compression of the root between a protruded disk and a hypertrophied ligamentum flavum. In the presence of an anomaly in which the cul-de-sac terminates higher than usual, it may be impossible to prove or disprove the presence of a protruded lumbosacral intervertebral disk by roentgenologic methods. It is interesting that all errors of interpretation occurred at the lumbosacral junction, where the spinal canal is relatively large and the diameter of the caudal sac may be small because of its fusiform termination. Under such circumstances even a large protruded disk may exist without indenting the sac.—*S. G. Henderson.*

Love, J. Grafton. Protruded intervertebral disks. *J. Am. M. Ass.*, Dec. 2, 1939, *113*, 2029–2034.

Analysis of more than 300 proved operative cases justifies the statement that laminectomy accompanied by removal of the protruded portion of an intervertebral disk is possibly the least radical of any known curative treatment for such a disabling condition. The characteristic symptom complex for protruded lumbar intervertebral disks is as follows: Complaint of intractable low back and sciatic pain. On examination, spasm of the lumbar muscles, loss of the normal lumbar lordosis, positive Lasègue's and Kernig's signs, sciatic tenderness and diminution or absence of the homolateral Achilles' tendon reflex. A moderate elevation of the total protein content of the cerebrospinal fluid. Narrowing of the fourth or fifth lumbar intervertebral space.

In spite of one's ability to diagnose the lesion accurately without the use of a contrast medium, in some cases routine employment of a contrast medium acts as a safeguard against overlooking multiple lesions, and enables the surgeon to perform as short a laminectomy as possible. However, direct exploration for protruded disk on the basis of a clinical diagnosis may be advisable even in the absence of positive roentgenologic findings.

Before undertaking such an operation, it is essential to know what disks are most likely to be involved and it is well to bear in mind that 10 per cent of all lesions were multiple in the series in which operation was performed. Ninety-six per cent of all protrusions in the aforementioned 300 cases occurred at the third, fourth or fifth lumbar vertebral interspace. In 84 per cent of the 300 cases the protrusions occurred at the fourth or fifth lumbar interspace. A removal of the laminae of the fifth lumbar vertebra and a resection of the fourth and fifth lumbar ligamenta flava will result in adequate exposure. If there is a protruded disk, its presence usually will be signalized by a marked thickening of the ligamentum flavum at that particular interspace. The important point to remember about the ligamentum flavum is that although it may be of sufficient size to compress the nerve roots, causing intractable pain, this phenomenon without an associated protrusion of the disk is rare. In 300 patients who had proved protruded disk, there were encountered only 12 cases of hypertrophy of the ligamentum flavum without an associated disk protrusion.

If the patient's symptoms are mild and do not interfere to any great extent with his usual activities, some one of the more common therapeutic measures may be employed. If the patient is very uncomfortable or is experiencing enough trouble to warrant bed treatment for two weeks, surgical treatment of the lesion should be advised. If radiopaque oil is used to localize the lesion, it should be injected into the lumbar segment and the roentgen examination should be carried out on the day of operation.

Recently the author has employed air in the subarachnoid space as an aid to roentgenologic localization of protruded discs, but the accuracy achieved by this method in his hands has not approached that resulting from the use of radiopaque oil.—*S. G. Henderson.*

Freiberg, Joseph A. Low back pain. *J. Am. M. Ass.*, Dec. 16, 1939, *113*, 2195–2198.

For years many orthopedic surgeons believed that the problem of low back pain was simple and that it was merely a question of differentiation between lesions in the lumbosacral area versus sacroiliac joints. However, there was actually a third lesion, the herniated or protruded intervertebral disc, previously unrecognized in its frequent rôle as a cause of low back pain and sciatica. At the same time that the herniated disc syndrome has become better known, so also have the intricate and less obvious muscular and fascial lesions about the lower part of the back, pelvis and thigh yielded to clinical and scientific study. In many cases early surgical treatment is to the great advantage of the patient, but in other series careful study of the individual patient will show that nonsurgical therapy alone is indicated in from 80 to 90 per cent of the cases. An active infectious lesion should be treated conservatively and a painful or unstable joint due to a pre-existing infectious process must be immobilized either by muscular or mechanical support or by operative fixation.

The real diagnostic problem in low back pain, with or without sciatica, is to differentiate between the primary and secondary causes for the pain and to evaluate their relative significance with regard to therapy. Dissimilar lesions may be and are associated with similar types of muscle spasm responses. Likewise, as the muscle spasm, per se, may be painful or may cause secondary painful areas, it is frequently difficult to differentiate between the primary lesion causing the muscle spasm and the secondary lesion, which is sometimes the true cause of the pain. The primary lesion associated with low back pain may be a true joint lesion, synovitis, a ligamentous trauma, periostitis at the site of muscle origin or insertion, myositis, fasciitis or a lesion of the intervertebral disc.

Before an attempt is made to treat a syndrome involving low back pain the lesion must be identified. The history of the mode of onset is especially important. In many cases the history will clearly bring out the fact that there was a single site of pain and tenderness, subsequently masked by the gradual development of secondary symptoms. The story of something slipping or snapping usually indicates a ligamentous or periosteal tear which may well be the lesion to be treated.

In the presence of acute low back pain with or without sciatic pain an extensive physical examination accompanied by forceful testing of the range of mobility of the various joints is definitely contraindicated. Observation and palpation will elicit the location of the areas of tenderness and injury. The more severe low back injuries may be accompanied by lesser fractures involving articular processes, laminae or pedicles. Lesions such as ruptures of the annulus fibrosus and consequent posterior protrusions of the intervertebral discs and the less frequent lesions of the ligamentum flavum followed by hypertrophy or cicatricial thickening of the ligament may occur and may be associated independently with constant or recurring attacks of low back pain. It may be assumed that many conditions about the lower part of the back are capable of causing painful manifestations and that because of the intricate mechanism of this region no one type of lesion can be accepted as the chief etiologic factor.

Acute aggravation of pain in the lower part of the back, buttock or sciatic nerve area accompanying sneezing or coughing may be due to a protruded disc or other mechanical pressure on the nerve root, or to spasmodic contracture of the abdominal and back muscles where there are lesions of the fasciae, muscles or joints. Relief from pain and disappearance of muscle spasm on lying down generally imply that a postural or abnormal mechanical strain has been removed from a lumbosacral or sacroiliac joint. The significance of the straight leg-raising or Lasègue test is discussed. The Ober test for contractured thigh fascia may be positive as the result of muscle spasm involving the tensor fasciae femoris and gluteal muscles. The

Ely, or prone knee flexion, test is one of the most valuable maneuvers to demonstrate the existence of thigh fascial contractures but not of a lumbosacral lesion, as originally described. Probably the most valuable of all the tests in determining the exact site of periosteal, ligamentous or joint lesions is the localization of one or more areas of definite tenderness on palpation when the patient is lying comfortably on a firm table. Relief of pain on injection of procaine hydrochloride usually demonstrates the fact that the lesion involves periosteal or ligamentous tissues previously the seat of a trauma or inflammatory process. In both neurologic and roentgenologic studies the spinal studies must be correlated with the other clinical data. —*S. G. Henderson.*

Engel, D. Dysostosis multiplex: Pfaundler-Hurler syndrome. *Arch. Dis. Childhood*, Sept., 1939, *14*, 217–230.

In 1919 Hurler described in detail 2 cases of dysostosis multiplex which had originally been reported by Pfaundler. They displayed the following unusual combinations of congenital anomalies: clouding of the corneas, a deformity of the skull (oxycephaly), a disproportionate dwarfism strongly resembling that of hypothyroidism (with some of the usual signs of that condition such as saddle nose, mental defect, dry skin, inguinal and umbilical herniae, crura valga and pedis valga), contraction of the fingers, limitation of movement in other joints and defective hearing. Pfaundler suspected he was dealing with a new syndrome and since then twenty other cases have been reported, showing the same combination of anomalies.

Engel's patients were two brothers, native Chinese, and he believes them to be the first cases of this condition observed in China. In addition to the other anomalies described in the literature, the brothers had bilateral congenital elevation of the scapulae, Sprengel's deformity. He considers the name of dysostosis multiplex to be more suitable than the previously proposed term, gargoylism.—*R. S. Bromer.*

Traub, Erich. Epiphyseal necrosis in pituitary gigantism. *Arch. Dis. Childhood*, Sept., 1939, *14*, 203–216.

Traub reports a case of pituitary gigantism. The patient's roentgenograms showed multiple epiphyseal necroses. The changes noted were a typical osteochondritis deformans of the right hip joint, Köhler's disease of both tarsal scaphoids, changes in the bodies of the vertebrae and epiphyseal necrosis in the heads of the first metatarsals. Traub thinks that these abnormalities were caused by endocrine dysfunction. Osseous involvement resembling Perthes' disease has been described in the literature in cases of adiposogenital dystrophy, in hyperthryoidism, in cretinism, in pituitary dwarfism and in gigantism.—*R. S. Bromer.*

Knutsson, Folke. Die röntgenologische Frühdiagnose der Rachitis. (The early roentgen diagnosis of rickets.) *Acta paediat.*, 1939, *24*, 403–421.

Knutsson examined roentgenologically the hands and feet and the anterior borders of the ribs of premature infants during their first year of life. In 36 cases he found rachitic changes. In 10 of these cases the rachitic changes were confined to the ribs only, the other metaphyses being normal. In 18 cases the rib ends were affected earlier than the other metaphyses and in 17 cases the ribs ends showed changes simultaneously with the distal ends of the diaphyses of the ulnas.

He believes that in many instances the rachitic process is fully manifest in the rib ends when the distal ends of the ulnas show only early or slight changes. Again changes may be present in the ribs and the skeleton elsewhere will show no roentgen evidence of the disease. The ends of the ribs become deformed very early, the most pronounced change being cupping or assumption of a beaker shape. In the ulna and fibula, the earliest change consists of a beginning bowl-shaped deepening of the metaphyseal border with a blurring of its contour. In the tibial metaphysis, the first sign is a tendency to spur formation of the metaphyseal border and the beaker shape or cupping is a later development.

Knutsson employs an oblique projection of the central ray for demonstration of the anterior ends of the ribs and thus prevents the overlapping of the shadows of the ends of both the right and left ribs which is found in straight lateral views.—*R. S. Bromer.*

ROENTGEN AND RADIUM THERAPY

Proske, Eva. Untersuchungen über Ösophagusmetastasen. (Studies on metastases into the esophagus.) *Strahlentherapie*, 1939, *64*, 227–248.

In the material of the Roentgen Institute of the University of Zurich the author observed in

tumors of the pharynx in which the primary tumor could be made to disappear chiefly by the use of the protracted fractional irradiation, the frequent development of secondary esophageal tumors.

The secondary esophageal tumors were observed chiefly in deeply situated mesopharynx tumors as well as in tumors of the posterior wall of the hypopharynx.

Secondary esophageal tumors were never observed when the primary malignant tumor was situated in the larynx and in the epipharynx. Secondary esophageal tumors are rare also in primary carcinoma of the mouth cavity.

Twenty-one cases of secondary esophageal tumors were found in 382 cases of meso- and hypopharynx tumors; one of these tumors was found before the discovery of a hidden mesopharynx tumor, 3 were found at the beginning of treatment of the pharyngeal tumor and the remainder only after the completion of the treatment of the primary tumor. The statistics presented above, however, give an erroneous picture since many patients died before the esophageal metastasis came to manifestation. A more reliable picture is obtained when the frequency is computed on the basis of patients rendered free of symptoms who are still alive or who have died as a result of distant metastases. Using this as a value a frequency of 16 per 141 patients during a period of observation of two years is obtained. This represents a frequency of about 11 per cent. It appears even more plausible to assume that every sixth to seventh patient who has been treated or cured of a meso- or hypopharynx tumor develops or dies from a secondary esophageal tumor.

The secondary esophageal tumor is always observed in carcinoma and never in sarcoma.

In 9 cases the histologic structure was identical with that of the primary tumor and in 1 case it was different.

No relationship exists between the size of the primary tumor and the appearance of the secondary esophageal tumor.

No relationship exists between the appearance of the tumor in the esophagus and regional metastasis of the pharynx tumor and the beginning of treatment.

The most frequent seat of the metastasis into the esophagus is the middle and lower third of the esophagus.

No relationship exists between the appearance of distant metastases outside of the esophagus and the secondary esophageal tumor.

In a predominant number of cases the secondary esophageal tumors appear as inoculation metastases in the esophagus. The lymphogenous mechanism of origin is rare.

The prognosis is hopeless.

The treatment is palliative and best results are obtained from roentgen therapy followed by radium.

The fact that esophageal metastases in the author's material were found even more frequently in association with a small primary tumor than with a large one suggests the possibility that the exploratory excision of part of the tumor favors the inoculation and may actually be responsible for it. In consideration of the above it would be very advisable to carry out the exploratory excision, if possible at all, by means of the electrosurgical loop.—*A. S. Schwartzman.*

Mallet, Lucien. Über die Teleröntgentherapie von Krebsmetastasen. (Teleroentgen therapy of carcinoma metastases.) *Strahlentherapie*, 1939, *64*, 201–218.

An attempt was made by this author to utilize teleroentgen therapy for the treatment of distant metastases, especially of bone metastases. This task, which seemed impossible of solution a few years ago, could again be considered with the recognition of the fact that the organism can tolerate whole radiations or half radiations when only slight individual doses are chosen and when the treatment is extended over a long period of time.

This newly recognized fact was utilized at first in the treatment of blood diseases, especially of lymphatic and myeloid leukemia, erythremia and especially of lymphogranulomatosis. Especially in the last mentioned disease it was found that after relatively very small doses distributed over the entire body the glandular enlargements disappeared.

It appeared conceivable also that some epithelial tumors could be successfully attacked by this method. Daily small doses given over a long period of time and distributed over the entire body were hitherto considered unsuitable because most radiologists were of the opinion that only the so-called cancericidal dose alone was effective.

Since the metastasis and generalization represent characteristic properties of carcinoma, an attempt must be made to adjust the radiation technique to this fact. Hitherto only local radiations were carried out. Clinical experience

has taught, however, that carcinoma is not a local disease and that even small originally operable and movable tumors metastasize relatively early. As mentioned previously, however, no attempt was made for a long time to treat the entire body because of the idea of cancericidal dose.

In 1932, however, Mallet determined clinically and experimentally that daily irradiation of a large region of the body with small doses are well tolerated by the individual. He further found that certain generalized carcinomas such as seminoma and myeloma can be destroyed by roentgen doses which were considered hitherto absolutely insufficient for the destruction of a tumor. The basis of teleroentgen therapy is as follows: The treatment of the primary tumor and of all its metastases is carried out by irradiation of large body regions, including the bony system, glandular tissues and viscera. An attempt is made in this form of therapy to obtain a cure of the carcinoma by means of a minimal dose of roentgen rays and an attempt is made to prevent, if possible, any injury to the hemopoietic system. Care is exercised also not to injure the skin and connective tissue in that daily only very small partial doses are used. Experience has shown that even minute doses have a definite detrimental effect on carcinoma. The effect of teleroentgen therapy is based on three physical conditions: The great distance, the large radiation field and the strong depth effect. An extensive region of the body is more or less uniformly permeated by roentgen rays. All body regions in which carcinoma metastasis is suspected are irradiated with the same amount of rays. The distance of the source of the roentgen ray must be so large that the rays fall practically parallel. The skin focus distance must be at least 1 meter and in some cases it actually varies from 1 to 3 meters. The field size on the skin must be at least 40×40 cm. The above represents basically teleroentgen therapy. One of the prerequisites for satisfactory results of teleroentgen therapy is the distribution of small doses over a very long period of time. The author irradiates his patients mostly daily but at least four times a week if the general condition of the patient permits it. The treatment of the thorax requires, for instance, at least 30 to 40 individual irradiations; that is, a duration of treatment of about two months where the patient is given daily about 25 r. When the entire body has to be treated a duration of four to five months is necessary.

Since 1933 over 600 cases of carcinoma have been treated by Mallet by teleroentgen therapy; the carcinoma was represented by extensive glandular infiltrations in the axilla, in the infra- and supraclavicular and cervical regions, in the mediastinum and in the pelvis, as well as by multiple bony metastases including the spinal column, pelvic girdle and upper and lower extremities. Even though statistical data cannot be offered which would show in a clear cut manner that many of these patients have been cured, nevertheless it can be definitely shown that in most of the patients treated by this method life was prolonged and the symptoms were ameliorated.—*A. S. Schwartzman.*

Mardersteig, Klaus. Röntgenschädigung und Blutbild. (Roentgen injury and blood picture.) *Strahlentherapie*, 1939, *64*, 311–317.

It has long been known that the hemopoietic organs are especially sensitive to roentgen rays. An individual is endangered even when exposed to the influence of very minute amounts of radiation in the course of a number of years; even under these conditions such minute injuries may lead to severe blood diseases such as aplastic anemia, myeloid and lymphatic leukemia. Even though the relationship between the radiation effect and anemia can no longer be doubted, the same does not hold true in regard to leukemia. Cases where roentgenologists have died from leukemia, of the myeloid or lymphatic type, are not as numerous as death due to anemia. Recent studies have contributed considerably to our knowledge of the white blood picture. Gansslen demonstrated regional differences in the normal white blood picture and has shown that the normal range of variation of the total leukocyte count as well as of the differential count is greater than hitherto stated even in textbooks. Gansslen carried out his studies on numerous patients as well as on a number of healthy individuals. From a study of 160 healthy maids he found that the white count under normal conditions varies not between 6,000 and 8,000 as hitherto stated, but between 3,500 and 9,000 and that the lymphocyte percentage varies not between 20 and 25 as hitherto assumed, but between 20 and 45. The lowest leukocyte count under normal conditions was found by him to be 2,700 and the highest lymphocyte count under normal conditions was found to be 50.5 per cent. In 40.6 per cent of these 160 healthy maids, a leukopenia was found. More or less similar results were ob-

tained by him from a study of 69 nurses and laboratory workers; the leukocyte count here varied between 3,500 and 7,500 and the percentage of lymphocytes between 20 and 50; also here a leukopenia was obtained in 50.5 per cent. In these cases the lowest leukocyte count was 3,500 and the highest lymphocyte percentage was 50.5.

Especially interesting were the results obtained by the same author in the course of the last twelve years from a study of 344 physicians, nurses and technicians of the Holfelder Roentgen Institute. The leukocyte count in these cases varied between 4,000 and 8,500 and the lymphocyte value between 20 and 45 per cent. A leukopenia was found in 46 per cent of the cases. The lowest leukocyte count obtained was 3,500 and the highest lymphocyte value was 57.5 per cent.

Gansslen definitely demonstrated the climatic and geographic influences on the white blood picture. These observatoins clearly show that the leukocyte and lymphocyte values in the healthy individual are subject to greater variations than hitherto assumed. Slight quantitative changes in the white blood picture appear, therefore, not as pathologic but as physiologic reactions. They may be explained by the dynamics of the blood regulation dependent on the vegetative nervous system which in its turn is intimately related to the hormones. The important recognition of the normal variations in the white blood picture are essential for the evaluation of blood injuries observed in the personnel associated with roentgen rays. This author is of the opinion that a leukocyte count of 3,500 and a lymphocytosis up to 60 per cent observed in a radiologist or a roentgen technician should no longer be looked upon as pathologic. Also the quantitative deviations of a slight degree found in the remaining blood picture should not be looked upon as roentgen injuries but should be considered as due to vegetative nervous reactions which have nothing to do with the radiation effect and which are not pathologic. However, if the leukocyte count is below 3,500 and the lymphocyte value exceeds 60 per cent, the findings should be considered as pathologic and if observed in radiologists or roentgen technicians should be related to the effect of roentgen rays. If the above are found in association with a pronounced shift to the left in the white blood picture as well as the presence of individual myelocytes and myeloblasts, then the findings point clearly to a radiation injury. Findings of the last mentioned type are usually associated with changes in the red blood picture expressed in the form of anisocytosis, poikilocytosis, polychromasia and an increased number of reticulocytes as well as of the normoblasts.—*A. S. Schwartzman.*

Bauer, R. Zur Kenntnis der Strahlenschädigung der menschlichen Lunge. (Contribution to our knowledge of radiation injury of the human lung.) *Strahlentherapie*, 1939, *64*, 249–266.

The author reports a case of roentgen injury to the lung which led to death, which he discusses from the clinical-roentgenologic viewpoint. A mediastinal tumor which extended in the left upper field, in all probability a thymogenic carcinoma, was given three series of roentgen treatments. The author reports exactly and in detail the course of the disease, the size of the dose and the time of irradiation. The autopsy revealed besides the extensive radiation induration of the lungs which led to death, also a large indurated body in the upper mediastinum in which tumor cells were no longer demonstrable.

In his report the author discusses extensively the literature dealing with the subject and the conditions under which such severe radiation injuries to the lung may occur. Besides the size of the roentgen dose and the intervals between the irradiation other conditions also, especially inflammatory processes in the lungs, favor the development of the radiation injury. A special predisposition to an inflammatory connective tissue reaction of the lung peculiar to a given individual may play an important rôle. In consideration of the fact that because of the anatomical structure of the thorax the actual percentage of the deep radiation dose cannot be determined with absolute certainty, excessive care is recommended in roentgen irradiation of the thorax.—*A. S. Schwartzman.*

Schairer, E., and Krombach, E. Röntgenstrahlenschädigung der Lunge mit tödlichem Ausgang. (Roentgen injury of the lung with fatal termination.) *Strahlentherapie*, 1939, *64*, 267–290.

A woman, aged thirty-nine, was subjected to intensive roentgen irradiation because of a mediastinal tumor; under the influence of this irradiation there occurred a complete indurative transformation of the tumor and a destruction of all tumor cells.

Death of the patient occurred as a result of a pulmonary injury produced by the roentgen rays.

An attempt was made by the authors to delimit the picture of pulmonary injury resulting from roentgen rays on the basis of their personal observations and on the basis of the cases reported in the literature. Attention is called to the fact that besides the latent period two stages must be principally differentiated: the main reaction with the more or less acute inflammatory processes and the stage of regression with connective tissue proliferation. In men, however, these two stages cannot be as distinctly differentiated because of the prolongation or spread of the radiation.

The pathogenesis of the pulmonary changes is considered by these authors on the basis of Richer's vascular theory. By the aid of this theory the differences in the pathologico-anatomical and clinical findings obtained by the various authors may be easily explained.

These authors do not accept the designation of Desjardins' "roentgen pleuropneumonitis" applied to this type of pulmonary injury. These authors prefer the designation of "acute or chronic pneumonia resulting from roentgen irradiation."—*A. S. Schwartzman.*

BUHTZ, HELMUT. Über Schädigung des Darmes bei Röntgenbestrahlung. (Injury to the intestines by roentgen rays.) *Strahlentherapie*, 1939, *64*, 291–310.

The author reports the history, clinical course and autopsy findings of 3 cases of injury to the intestines by roentgen rays. Macroscopically in all these cases there developed a pronounced ulcer formation in the intestines. The histologic examination revealed necrosis of the intestinal wall of a variable degree, in some cases leading to a complete wall defect with fibrosis of the submucosa and occasionally hyperplasia of the muscularis, injury to the serosa, slight infiltrations of a chronic inflammatory type and especially vascular changes in the form of slight endarteritis and in some cases a total endophlebitis obliterans. These intestinal injuries were found also in the neighboring macroscopically appearing intact, intestinal regions.

For the verification of the diagnosis of roentgen injury the findings were compared with similar findings in the intestine in other diseases such as tuberculosis, dysentery, intestinal lues, uremia, endemic sprue, coprostasis and lymphogranulomatosis. The author also compares the histologic findings made in his cases with those reported in the literature and discusses the topographic localization of the injuries which he relates with the peculiarities of the radiation process.

The author discusses cases of a similar nature reported in the literature and considers the causes which may lead to a roentgen injury of the intestine; he considers in detail the physical properties of roentgen radiation and the possibility of a combination injury based on conditions such as peculiarity of the tissues resulting from predisposing factors or from some vascular injuries which have influenced the end-results of the roentgen rays; he also considers the general biological effect of roentgen rays.—*A. S. Schwartzman.*

CHAOUL, H. Bisherige Ergebnisse der Röntgennahbestrahlung freigelegter Rektumkarzinome. (Results hitherto obtained in the treatment by close roentgen irradiation of exposed carcinoma of the rectum.) *Strahlentherapie*, 1939, *64*, 219–226.

In a previous communication the author reported the results obtained in the treatment of 8 patients suffering from inoperable carcinoma in which a disappearance of symptoms was obtained following an exposure of the carcinoma and a close roentgen irradiation. This method is essentially a combination of surgical and roentgen treatment. The surgical treatment consists in the direct exposure of the tumor so that it can be reached by the rays similarly to a superficially situated tumor. The surgery consists basically, therefore, in a resection of the coccyx and lower segment of the sacrum after which the rectum is mobilized, split and its two borders are fixed into the skin wound by sutures. The tumor exposed in this manner is then subjected to roentgen irradiation. The diseased region is irradiated daily with doses varying from 150 to 500 r. The irradiation is continued until the tumor has disappeared completely. To achieve this, in the author's practice, a total dose of 12,000 to 15,000 r was found necessary. The author emphasizes the absolute necessity, in treatment of this type, of fractionating the dose since this, he believes, makes possible the sterilization of the carcinoma cells. As a rule towards the end of the treatment there occurs a reaction of the mucosa manifested in the form of a deposit on the irradiated region of the intestinal mucosa. The duration of this phenom-

enon lasts from six to eight weeks and in unusual cases it may last even a few months. Occasionally also the intestinal wall reacts in the form of a sclerosing edema which may eventually require surgical treatment.

Employing this method 23 patients, practically all of which had inoperable carcinoma of the rectum, were treated.

In 14 of these a complete disappearance of the tumor was obtained. Two of these patients were under observation for about four years, 1 for three years, 3 for two years and the remainder for over one year. In all the successfully treated patients a gain in weight of 20 to 40 pounds was obtained. In all the cases which were subjected to a restorative surgical operation following the disappearance of the tumor a normal intestinal function was obtained. In consideration of the hopelessness of cases of this type the author considers the results presented above as satisfactory.—*A. S. Schwartzman.*

Walther, O. Resultate der Strahlenbehandlung bei Sarkomen. (Results of radiation treatment in sarcoma.) *Strahlentherapie*, 1939, *64*, 59–112.

Between 1919 and the end of 1936, 240 cases of sarcoma were treated and followed up in the Roentgen Institute of Zurich; 132 of the cases were males and 108 females and the average age of the patients was 44.8 years. In this number cases of solitary giant cell tumor, cases of lympho-epithelial tumor and melanoma were not included. The distribution of the sarcoma in the cases studied was as follows: 19 per cent along the digestive tract, 16 per cent along the supporting tissues with the exception of the bony system, 14 per cent in the bony system, 13 per cent in the region of the respiratory tract, 12 per cent in the region of the thyroid gland, 9 per cent in the region of the lymph node system, 7 per cent in the region of the genitourinary tract and 2 per cent in the mammary glands. In 91 per cent, or 219 cases, the diagnosis was verified histologically and was as follows: round cell sarcoma in 37 cases, lymphadenoid sarcoma in 36 cases, spindle cell sarcoma in 32 cases, polymorphocellular sarcoma in 27 cases, sarcoma without more distinct differentiation in 26 cases, fibrosarcoma in 14 cases, hemangio-endothelioma in 12 cases, Ewing's sarcoma in 10 cases, reticulo-endothelial sarcoma in 9 cases, osteogenic sarcoma in 6 cases, myxofibrosarcoma in 5 cases, plasmocytoma in 4 cases and myeloma in one case. In 9 per cent, or 21 cases, no histological verification was obtained.

Of the 240 cases, 38, or 16 per cent, were treated surgically-radiotherapeutically and 202, or 84 per cent, were treated exclusively by radiation therapy. In 145 of the 202 cases, or 72 per cent, at attempt was made to obtain a cure by radiation therapy and in 57 patients, or 28 per cent, the irradiation was given for palliative purposes purely, since a cure could no longer be expected.

Two hundred thirty-seven of the 240 cases have been followed up in the course of one year after the treatment. Of these 69, or 29 per cent, were free of symptoms; 223 cases were followed three years after the treatment and of these 44, or 20 per cent, were found free of symptoms, while 201 cases were followed five years after the treatment was terminated and of these only 26, or 13 per cent, were free of symptoms.

Of the 240 cases only 31, or 13 per cent, were in an operable stage at the time radiation therapy was instituted, while 209, or 87 per cent, were in the inoperable stage. The results obtained in the operable cases were as follows:

Nineteen of the 31 cases, or 63 per cent, were free of symptoms after one year; 14 cases, or 56 per cent, were free of symptoms after three years and 7 cases, or 35 per cent, were free of symptoms after five years. Of these 31 cases only 1, a bilateral round cell sarcoma of the mammary gland, was locally cured by the exclusive use of radiotherapy but died from a generalized metastasis. The remaining 30 cases were first operated on and then given radium therapy.

Two hundred five of the 209 inoperable cases could be followed up and the results obtained were as follows:

Forty-eight of the 205 cases, or 23 per cent, were free of symptoms after one year; 29, or 14 per cent, were free of symptoms after three years, and only 10 per cent were free of symptoms after five years.

The best results, judged on the basis of a five year follow up study, were obtained in cases of tumors of the eye region, ear region, mouth cavity, mesopharynx, mediastinum and the supporting structures of the body. The permanent cures here exceeded 25 per cent. In other localizations either slight or no permanent cures were obtained.

One hundred eighty-one of the 240 cases of sarcoma, or 75 per cent, died as a result of the disease; 113 of these, or 62 per cent, were favor-

ably influenced palliatively. The average duration of life of the patients who died following irradiation from neoplasms was 12.2 months. Good palliative results were obtained in tumors of the accessory nasal cavities, of the epipharynx, mesopharynx and of the mediastinum. Poor palliative results were obtained in tumors of the kidneys, colon and urinary bladder.—*A. S. Schwartzman.*

MAYER, A. 30 jahrige Erfahrungen über Uteruskarzinom-Therapie. (Experience of thirty years with therapy of uterine carcinoma.) *Strahlentherapie*, 1938, *63*, 407–413.

The curative results in cases of uterine carcinoma obtained in various clinics vary considerably and are therefore not always comparable. In consideration of the above it appears desirable to discuss the results obtained in the treatment of uterine carcinoma in the course of the last twenty years by the author and the results obtained by Döderlein in the course of ten years which were followed up by the author.

The methods of treatment employed during these years were as follows: pure surgical, surgery combined with prophylactic after-irradiation, preliminary irradiation followed by surgery and pure irradiation.

The present report, therefore, deals with the results obtained from these various methods. Altogether 1,900 cases of carcinoma of the cervix were treated. The criterion of the results obtained was based on the absolute permanent cure, the surgical mortality and the working ability of the patients in inoperable cases. An absolute permanent cure of the cases observed was obtained in about 20 per cent and a relative cure in the surviving operated patients was obtained in 39.3 per cent. The primary surgical mortality varied between 18 and 20 per cent.

An attempt was made to improve the surgical permanent cure and therefore surgery was complemented by prophylactic after-irradiation. In 85 cases where this method of treatment was employed the relative cure of 39.3 per cent was increased to 47 per cent. Next an attempt was made to decrease the primary surgical mortality. In nearly 50 per cent of the cases death was due to peritonitis. To eliminate this a prophylactic preliminary irradiation was carried out. In 91 cases where this treatment was used the total postoperative mortality was only 4.3 per cent and the mortality due to peritonitis proper was only 1.1 per cent.

Eventually the radium-roentgen treatment was basically employed. For purposes of evaluation of the results obtained, 147 cases were available with an operability of 48 per cent. The relative cure obtained in these cases was 46.9 per cent in comparison with the 47 per cent obtained from surgery. Otherwise, however, irradiation was found preferable to surgery, since the irradiation has practically no primary mortality, and is employable in each case including the inoperable cases. Irradiation also gives a better absolute cure, namely, 30 per cent in comparison with 20 per cent obtained from surgery and a relative cure of 17.4 per cent in the inoperable cases. The data presented above clearly show the full justification of radiation treatment of carinoma of the uterus. It is not only not inferior to surgery, but in some respects actually superior.

The operability of carcinoma of the body of the uterus as judged on a study of 450 cases was found to be equal to about 80 per cent. The postoperative mortality in these cases was 9.6 per cent. The absolute cure obtained in all the observed cases was 46 per cent. With the addition of the prophylactic after-irradiation employed on 124 cases, an absolute cure of 48 per cent was obtained. A relative cure of the operative cases was obtained in about 60 per cent, and was therefore considerably higher than in cases of carcinoma of the cervix. Contrary to the results obtained from surgical treatment by means of pure irradiation, an absolute cure was obtained in only 33 per cent, therefore inferior results to those obtained from surgery. In consideration of the results obtained this author recommends and actually employs surgery as a rule in cases of carcinoma of the body of the uterus and only exceptionally uses irradiation. The following conclusions are drawn by the author:

Roentgen-radium irradiation is the usual method of treatment in carcinoma of the cervix. Surgery must be considered in carcinoma of the uterus, in rare cases of carcinoma of the cervix during pregnancy in carcinoma of the cervical os or the so-called central carcinoma nodules which are frequently the adenocarcinoma type, and in carcinoma of the cervix of young women which appears especially malignant. As a second choice surgery is considered in carcinoma of the cervix refractory to roentgen rays which do not respond sufficiently six to

eight weeks after the irradiation, in cases where an apparent cure has been obtained from irradiation but where a bloody, foul smelling discharge persists pointing to a carcinoma in the deeper regions, in the rare cases of radiogenic vaginal stenosis where a bloody or foul smelling discharge points to carcinoma in the deeper regions and in the occasional operable carcinoma recurrences following irradiation.—*A. S. Schwartzman.*

Schmiemann, Rolf. Ergebnisse der Strahlenbehandlung des Uteruskarzinoms an der Würzburger Universitäts-Frauenklinik. (The results of radiation treatment of carcinoma of the uterus at the Würzburg University Women's Clinic.) *Strahlentherapie*, 1938, *63*, 583–613.

The author reports the results obtained in the course of nine and a half years, from January 1, 1924 to July 1, 1933, from pure radiation treatment of uterine carcinoma employed in the Würzburg University Women's Clinic. The treatment consisted always in a combined application of roentgen and radium rays. The report of the results is based on the accepted standards for statistics dealing with carcinoma as suggested by Winter and Voltz. Special attention has been paid not only to the data dealing with restoration of efficiency or cures, but also to the mortality and to the duration of life of the irradiated carcinoma patients. A classification according to age revealed a clear cut predominance of the fifth decade over all other age groups. No difference could be obtained regarding the results from irradiation as related to different age groups.

A comparison of the results obtained in different clinics from radiation therapy and surgical treatment in uterine carcinoma, as reported in the literature, revealed a definite superiority of the results obtained in the treatment of carcinoma of the uterine cervix in the University Clinic of Würzburg, in comparison with the results obtained in other clinics from pure radiation treatment or pure surgical treatment. No such clear cut superiority could be demonstrated in regard to the results obtained from the treatment of carcinoma of the uterus. Even though a definite answer to the question whether radiation treatment or surgery should be employed in carcinoma of the uterus cannot be given, nevertheless, in consideration of the developmental possibilities of radiation therapy, in comparison with the possibilities of surgery which has practically already reached its peak, the author is inclined to state that he believes in the great future of pure radiation therapy.—*A. S. Schwartzman.*

Caffier, P. Ergebnisse und Erfahrungen der Kollumkarzinombehandlung mit besonderer Berücksichtigung der Radiumtherapie. (Results and experiences in the treatment of carcinoma of the cervix with special consideration of radium therapy.) *Strahlentherapie*, 1938, *63*, 639–657.

The report deals with the results and experiences of Stoeckel's clinic in Berlin in the "selective" treatment of carcinoma of the cervix and the results are based on a study of seven years' duration. Of the 1,314 cases of carcinoma of the cervix treated during this time, an absolute cure was obtained in 28.9 per cent. A relative cure obtained by operation was demonstrated in 45.9 per cent (399 cases) and a relative cure obtained by irradiation was demonstrated in 21.9 per cent. The author discusses in detail the technique of the radium treatment of carcinoma of the cervix routinely employed in Stoeckel's clinic. The relative irradiation of the early cases of carcinoma (Groups I and II) was 35.8 per cent and was, therefore about 10 per cent below the cures obtained by operation, which points to the preferability of surgery. The efficiency of radiation therapy is especially imposing in the poor cases in which it still offers a permanent cure in about 13.2 per cent of the cases. The pure primary radium mortality was 1.5 per cent in the 905 cases treated in this manner, the infection mortality was only 0.7 per cent. The irradiation injuries referable to radium under the technique employed were demonstrable in only 3 cases in the form of an ulcerative proctitis.—*A. S. Schwartzman.*

Wasserburger, K., and Smereker, H. Die Radiumbehandlung des Gebärmutterhalskrebses. (The radium treatment of carcinoma of the uterine cervix.) *Strahlentherapie*, 1938, *62*, 584–600.

An attempt was made by the authors to determine the dosage distribution in radium therapy of carcinoma of the uterine cervix. This study was referred chiefly to the methods of treatment employed in the Radiological In-

stitute of Vienna in the form recommended by Forssell and Heyman, on one hand, and by Regaud, on the other hand. The dose measurements were carried out according to the condenser chamber methods of Sievert and the doses were reported in roentgens and in imc. h. In order to determine the dose which actually acts on the tumor the measurements were carried out in the immediate proximity of the applied radium preparation. The study of the distribution of this dose of rays on the greatest path of extension of carcinoma of the uterine cervix such as the parametrial tissue, the urinary bladder, rectum and the lymph nodes was carried out on preparations of cadavers. The results obtained from the dose measurements were compared with the clinical experience from the use of the radium therapy in the treatment of carcinoma of the uterine cervix. It was found during these studies that in order to prevent a pronounced change of the mucosa in either of the two methods referred to above, a new packing of the vaginal radium applicator is necessary. It was further found that in advanced cases of carcinoma of the uterine cervix a carefully planned roentgen irradiation following the radium application is necessary.—*A. S. Schwartzman.*

PICKHAN, A. Die intrauterine Radiumbehandlung der hämorrhagischen Metropathien. (The intrauterine radium treatment of hemorrhagic metropathy.) *Strahlentherapie*, 1938, *63*, 682–688.

A new period of special research and treatment of diseases dependent on animal germinal glands has been instituted with the discovery of the high radiosensitivity of these animal germinal glands. Especially the recognition of the relation of the so-called benign uterine affections with the disturbance in the ovarian activity led to the development of a procedure which at present may be looked upon as the method of choice in the treatment of these affections. There exists a large group of uterine hemorrhages which are not of a malignant origin but which frequently lead to conditions dangerous to the life of the patient, in which modern radiation therapy assumes a dominant position. Reference is had here to the hemorrhagic metropathia, especially the climateric and preclimateric hemorrhages the cause of which must be looked for in pure functional disturbances in the ovarian inner secretory activity.

The ovaries are glandular organs, the cells of which are in a constant state of development. With the progress of proliferation the radiosensitivity of the follicular apparatus increases. In the resting mature follicles the radiosensitivity is decreased. Two paths are accessible to therapy, namely a uniform destruction of all ovarian cells and a partial elimination of function of the most sensitive part of the follicular apparatus. Both these purposes can be achieved by deep roentgen therapy.

This author employs weakly filtered radium radiation in cases of hemorrhagic metropathies. This treatment is employed preferably in individuals of the preclimateric age. In all other cases of hemorrhagic metropathy of a benign cause, roentgen therapy is employed when no surgical indication exists. In regard to treatment, the author emphasizes the importance of a thorough history, with special attention to previous infectious diseases of the genital organs or their appendages. The treatment can not be employed in cases of recent inflammatory processes of the genital organs. In cases where there is a previous history of adnexal diseases, a careful control of the temperature of the patient is necessary. A thorough blood picture must be obtained. In each case an exploratory curettage must precede the treatment in order to exclude malignancy. The patient is prepared for the treatment in the course of two to three days after admission and this preparation consists in antiseptic treatment of the vagina, cervix and cervical canal by means of tampons soaked in antiseptic solution. The amount of radium employed is determined by the size of the uterine cavity. In most cases 30 to 50 mg. of radium is necessary and the radium is introduced under aseptic precautions. The average dose is about 1,500 mg. hr. The average age of the women treated in this manner is 43.3 years and in each case permanent amenorrhea is obtained on the average after 0.7 months.

Not in a single case did this method of treatment prove ineffective. Not in a single case were any undesirable side effects observed. Following each treatment, however, the patients should be under observation; especially during the first months after the treatment an occasional sounding of the uterine cavity is necessary in order to prevent any possible occlusions of the cervical canal and a consequent infection.

This type of treatment must not be employed in women suffering from chronic inflammatory

processes of the adnexa as well as in all cases with acute or chronic processes of the genitals. It must be remembered that in cases of the last mentioned type also percutaneous radium therapy is not without danger.

It is surprising how soon after the radium treatment the general condition of the patient improves and the patient is in a position to return to work. The author believes, on the basis of his experience, that intrauterine weakly filtered radium therapy is the method of choice in the treatment of preclimateric hemorrhages. —*A. S. Schwartzman.*

Crainz, Franco. Die Behandlungserfolge bei den bösartigen Eierstocksgeschwülsten. (The results obtained in the treatment of malignant tumors of the ovaries.) *Strahlentherapie*, 1938, *63*, 434–464.

1. Each case of a malignant tumor of the ovaries must at first be operated on; if a complete surgical removal of the tumor is impossible, as much of the tumor as possible should be removed.

2. In cases where the tumor is present only on one side, the second ovary, which may be perfectly healthy, must also be thoroughly removed. The uterus should be left intact.

3. In each case radiation therapy should be given after the operation even when the entire tumor has apparently been removed. As much as possible it should be given in the form of a homogeneous roentgen irradiation of the pelvis and lower abdomen and an additional intrauterine radium application should be carried out.

4. In those cases where no surgery can possibly be carried out, irradiation should be employed if the general condition of the patient permits it. Also in cases of this type a combined roentgen-radium irradiation is desirable.

5. The results obtained from the treatment carried out according to the above given method in the University Clinic of Würzburg are better than any hitherto reported in the literature. Of the 152 patients with malignant tumors of the ovaries observed, 23.7 per cent were still alive after five years; of the 131 treated cases, 27.5 per cent were still alive after five years. Of the 38 cases where the tumor was thoroughly removed surgically, 60.5 per cent were still alive after five years. Of the inoperable cases (incompletely surgically removed tumors and postoperatively irradiated or exploratory laparotomies and postoperatively irradiated or only irradiated cases), 14 per cent were still alive after five years; of the inoperable cases, 19.5 per cent were alive after five years of those where the tumor was partly removed while only 4.5 per cent of the cases remained alive after five years where the exploratory laparotomy was followed by irradiation; of those inoperable cases which were treated only by irradiation, 13.3 per cent were still alive after five years. Of all surgically treated carcinoma cases 25 per cent were alive after five years and of all the surgically treated sarcoma cases 100 per cent were still alive after five years.

6. The therapeutic results presented above are of especial value because they were obtained from a definite plan of treatment, because the results are classified on the basis of the different types of treatment and because the percentage of cases after five years' observation was determined.—*A. S. Schwartzman.*

MISCELLANEOUS

Crowther, J. A. Die biologische Wirkung der Röntgenstrahlen. (The biologic effect of roentgen rays.) *Strahlentherapie*, 1938, *62*, 569–583.

Experimental studies of the biologic effect of roentgen rays have been carried out since 1895. The literature dealing with this subject is extremely extensive. A study of this literature reveals that best results were obtained when the effects of roentgen rays were studied on simple systems. This author also limits himself to the study of the effect of roentgen rays on individual cells and unicellular organisms. Experiments of this type show an unusual variability of the radiation effect on different types of tissues. For instance, even a dose of 40 r may kill about 50 per cent of some unicellular organisms; on the other hand, a dose of 330,000 r is necessary in order to produce death of 50 per cent of the individuals of a *Colpidium* culture. An elimination of cell division may be obtained in tissue cultures with a dose as small as 120 r; on the other hand, a dose of 13,000 r is necessary in order to achieve a complete death of the cells. During cellular division the cells are more sensitive to roentgen rays, and rapidly growing non-differentiated cells are in general more sensitive than mature cells. Doses of roentgen rays capable of killing all types of living tissue are beyond 100,000 r. This effect, which is nonspecific, is no doubt based on chemical changes

in the cytoplasm produced by the changes in the tissues. Photochemical changes are demonstrable in many types of organic and inorganic substances when large doses of roentgen rays are used. The effect is chemically demonstrable following the use of a dose of 2,000 r, a dose, therefore, 50 times as strong is necessary in order to change the cellular cytoplasm to such an extent that it would produce death of the cell. It is not surprising, therefore, that a tissue culture may be led to death from the use of a dose of 100,000 r. On the other hand, it is quite surprising that in the same tissue only 1/1000th of this dose is capable of producing extensive biological effects.

The effect of some roentgen-ray doses may be classified in three groups: (1) elimination of the division ability of the cells; (2) production of mutations, and (3) in certain cases, especially in cells which divide rapidly, death.

Mitosis and mutations are functions of the cellular nucleus. The destruction in the rapidly growing tissues is probably conditioned by the inability of the irradiated cells to divide. In all probability, therefore, in each case the radiation effect does not involve the cell as a whole, but especially the cellular nucleus. Vitemberger demonstrated experimentally that in a resting stage the cellular nucleus is 25 times as sensitive to roentgen rays as the cytoplasm.

Experimental studies further justify the statement that the point of the radiation effect is not limited to the nucleus as a whole but to certain structures of the nucleus. The resting nucleus appears completely homogeneous. By means of the usual microscopic methods not a trace of the structural richness of the nucleus is demonstrable. According to the general view of cytologists the apparent uniformity of the nucleus actually exists. During this stage the cell is relatively slightly sensitive to roentgen rays. With the appearance of mitosis the characteristic cell division structures appear and especially during this stage of the life of the cell it is very sensitive even to small roentgen-ray doses. The appearance of cell division structures and the increased sensitiveness are doubtless not accidental in nature. Still more conclusive proof is obtained from experiments dealing with the radiation effect on the hereditary mass. An effect of this type cannot be reproduced to the same degree by any other agent. The gene theory of mutations is one of the best founded biological theories and each radiation effect must in the last analysis represent an effect on a gene. In this manner, the specific effectiveness of the roentgen rays on particles of submicroscopic dimensions is conclusively proved.

The relationships between the dose and biological effect have been very thoroughly studied. The results of these studies are usually represented in the form of curves which illustrate the percentage of the surviving individuals dependent on the radiation dose.

The explanations of the biological mode of action of roentgen rays may be classed into two main groups which may be briefly designated as the toxin and the "hitting" theories. According to the toxin hypothesis, the radiation produces as a result of a photochemical influence of the nuclear substance a nonspecific toxically acting substance which by way of diffusion into the neighboring tissue leads to the observable changes.

According to the "hitting" theory the effect of roentgen rays comes to manifestation when a sensitive biological structure is hit by the roentgen rays. Both theories are rather well substantiated. This author is of the opinion that basically the biologic effect of roentgen rays is to be explained by the changes in the electric charge proper. The appearance of the different structures at the beginning of mitosis is highly similar to the coagulation of colloid particles and it is known that the structures are electrically charged. The equilibrium between the differentiated and homogeneous phases of the nucleus must be very labile so that at a critical point a change in the charge is easily achieved and this change disturbs the entire course of the mitosis or disturbs the normal distribution of genes and thereby leads to a mutation. A few years ago this author, together with Fairbrother, showed that positively charged colloids may be destroyed by roentgen rays. The dose necessary for this purpose is relatively large but the colloids employed in these experiments were more distant from the isoelectric point than those occurring in the biological material. Recently this author, together with Liebmann, discovered the fact that even with a dose of roentgen rays as small as 20 r the electrokinetic potential can be changed by about 10 per cent. Changes of the potential of the colloid of a similar degree may produce definite biologic effects in the cellular nucleus. —*A. S. Schwartzman.*

Daels, Franz, Fajerman, H., and Vande-putte-van Hove, W. Wie sich beim Versuchstier eingespritztes lösliches Radium in den verschiedenen Körpergeweben verteilt. (The distribution of soluble radium in the various body tissues following its injection into the experimental animal.) *Strahlentherapie*, 1938, *63*, 545–555.

A series of experiments was carried out by the authors of the following nature: A white rat, inoculated with a sarcoma tumor of about 1.5 cm. in diameter, during an advanced state of pregnancy, was given subcutaneously daily in the course of three days in succession 1 cc. of a radium solution of 1:400,000, that is, 0.0075 mg. of radium. The animal was killed six hours after the last injection and many sections from various tissues were made for imbedding and drying. The following dried tissue when acting on a film in the course of seven days rendered the film black: bone, liver, kidney, fetus and skin region where the injection was made. After four weeks also blood and lung tissue rendered the film black. The appearance of the film was doubtful under the influence of spleen, placenta, amniotic fluid and stomach tissue. No effect whatsoever was obtained from sarcoma tissue, heart, suprarenal tissue, brain and muscle tissue. The imbedded tissue gave a weaker effect apparently as a result of the washing which preceded the imbedding. The tissues which, according to these experiments contained most radium, were bone, liver, kidney and fetus. The placenta, therefore, did not act as a storing organ and the tissue of the fetus retained more radium than the placenta.

In another experiment a pregnant guinea pig inoculated with sarcoma tissue was given some radium injection shortly before delivery, receiving altogether 0.02 mg. of radium. Seven hours after the last injection the guinea pig was killed. Also in this experiment the liver, kidneys and lungs were found to contain radium; also here the placenta and fetus contained radium and also here the placenta did not prevent the penetration of radium into the fetus. Numerous other experiments were carried out by these authors and the following results were obtained:

Pregnant and non-pregnant mice, white rats and guinea pigs were given soluble radium as well as various animals inoculated with sarcoma tumors. For purposes of demonstration of the radium in the tissues the roentgenographic picture was utilized. The films were subjected to the influence of the various organs in the course of one week up to three months. These studies have shown that the radium was found in largest amounts in the organs which are considered as excretory organs such as liver, kidneys and lungs, as well as in those which function as blood forming tissues, such as bony tissue, liver and spleen. The placenta and fetus both contained some radium and the placenta did not prevent the penetration of radium into the fetus. Sarcoma tissue does not contain excessive amounts of radium. Only traces and in some cases no radium was found in the muscle and brain tissue. The largest amount of radium was found in the bony tissue; relatively large amounts of radium were found in the liver and spleen and somewhat later also in the kidneys, intestines and lungs. Small amounts of radium are found in the sarcoma tissue and in the blood only during the first three days following the last radium injection.—*A. S. Schwartzman.*

Reding, R. Über den Einfluss von Eiweissabbauprodukten auf die Vorgänge bei der Krebsbildung. (The influence of protein decomposition products on the processes in carcinoma formation.) *Strahlentherapie*, 1938, *63*, 556–560.

It is generally assumed that two essential factors must cooperate in order to make possible the appearance of carcinoma, namely, the local factor: a cellular decomposition and regeneration focus, and the general factor: the predisposition. Below the author discusses the significance of protein bodies for the appearance of these two factors. Recent studies have substantiated the old observation that cellular destruction and regeneration precede the development of a carcinoma. It is at present an accepted fact that cellular dissolution foci and proliferation foci which correspond to the chronic ulcer formations may occur within the tissue frequently without actually producing a genuine ulceration. Under these conditions they represent the closed cellular dissolution and proliferation foci. In the mammary gland, for instance, there occurs under the influence of estrin an alternation between necrosis and proliferation. Similar conditions are found in indol poisoning in the bone marrow, in some parenchymatous organs under the influence of protein bodies and in the reticulo-endothelial system under the influence of tar. The various

carcinoma producing substances which differ vitally in their nature have, therefore, the same biological effect; that is, produce within the tissues latent foci of cellular dissolution and proliferation the effect of which is identical with chronic ulcerations. The similarity of the latent chronic cellular dissolution foci with chronic ulcerations permits a uniform definition of all carcinoma producing substances and enables the explanation of the localization of many deeply situated forms of carcinoma. In the local focus the protein bodies which originate during the cellular dissolution lead to the development of cellular proliferation. On the other hand, the absorption of protein decomposition products which reach into the circulation during the cellular dissolution leads to a definite intoxication of the body which represents the cause of the predisposition to carcinoma.

The predisposition to carcinoma implies the existence of relations which predispose and promote the appearance, propagation and the development of the peculiar metabolism of malignant cells. The following are the conditions which determine this predisposition: (1) Humoral changes, such as an alkalosis, an increased content in polypeptids, aminoacids, fibrinogens, globulins and cholesterin. (2) Functional disturbances; a diminished oxygen supply to the tissue, an increased glycolysis, disturbances in the blood sugar regulation, a paralysis of the reticulo-endothelial system, an increased water content of the tissue and a vagotonia. (3) Endocrine disturbances; hypertrophy of the anterior lobe of the hypophysis and a certain increase in the number and volume of the islands of Langerhans.

The pathogenesis of the general carcinoma predisposition seems, therefore, to consist of an intoxication of the body with protein decomposition products. These protein decomposition products are endogenous or exogenous in origin, depending on the fact whether they are derived from the body proper or from exogenous protein bodies. The exogenous intoxication occurs as a rule through the food intake. It has been proved that complex polypeptids may reach the peripheral circulation when the protein utilization by the liver is insufficient. An acute protein intoxication, digestive in nature, may appear as a result of intestinal obstruction which is followed by an excessive absorption. A chronic protein intoxication may occur in individuals who superficially appear healthy but who suffer from a liver insufficiency especially affecting the protein metabolism.

The work is concluded with the statement that the closed foci of cellular dissolution and regeneration are the analogies of chronic ulcers and with the statement that the humoral pathologico-anatomical and functional symptomatology of the carcinoma patients is not specific; similarly it is not irrelevant or secondary because it seems to present signs of a protein intoxication. The fact that many humoral changes appear exactly identical in carcinoma patients and in various other protein intoxications explains the fact why hitherto specific humoral changes have not been demonstrated in carcinoma patients.—*A. S. Schwartzman.*